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AN UNUSUAL CASE OF AMŒBIC DYSENTERY.[1]

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In descriptions of amœbic dysentery emphasis is always laid upon the occurrence of irregular, undermined ulcers as the most characteristic change in the large intestine. This form of ulceration is the only one exhibited in the two pathological museums which I have had an opportunity to visit. Furthermore, it is not common to meet with a case of amœbic dysentery, running an acutely fatal course, accompanied by profuse hæmorrhage. Such a course, together with unusually acute lesions of the large intestine, distinguished the following case which I examined while connected with the Biological Laboratory of the Bureau of Science in Manila.

M., a native Filipino, a patient in the Civil Hospital of Manila, had a severe and acute type of amœbic dysentery with abundant hæmorrhages from the bowels. He died, apparently from loss of blood, and came to autopsy December 28, 1906.

AUTOPSY NOTES.

Body of an adult male Filipino about 25 years old, sparely built; moderately well nourished; mucous membranes extremely pale; a few ecchymoses in the skin of arms and legs.

Subcutaneous fat.—Moderately abundant, very yellow.

Peritoneal cavity.—Clear, no adhesions; mesenteric glands large, pale, soft; on section pale, gray; structure visible.

[1] Read before the American Association of Pathologists and Bacteriologists, Boston, April 9, 1909.

Thorax.—Clear; lungs occupied less than one-half of thoracic cavity; were very pale and cushiony; uniform in appearance; normal on section; bronchi and pulmonary vessels clear.

Heart.—Pericardium clear; a number of pin-point ecchymoses around the auriculo-ventricular groove; muscle pale, firm, uniform; valves and endocardium normal; aorta clear.

Abdominal cavity.—Spleen moderately enlarged and firm; surface normal; on section trabeculæ prominent; the color distinctly pale. Liver of normal size, pale and firm; on the anterior surface of right lobe directly over gall bladder and 10 cubic centimeters from the anterior margin of the liver, a puckered scar was situated with adhesions to the anterior wall of chest. On section, the scar of an old sinus was found leading for 6 cubic centimeters to a firm, yellow-white scar near the center of the lobe. Right and left kidneys were alike, both large; the capsule stripped readily, leaving an extremely pale, soft cortex. On section, the cortex was extremely pale; the structure cloudy but otherwise normal; the pyramids were also very pale. The suprarenals, pancreas and stomach appeared normal. In the small intestine numerous *uncinaria* were found in the upper part where red points studding the mucosa were observed. In the lower portion several specimens of ascaris occurred; otherwise the small intestine was normal.

The large intestine contained a large amount of dark red, almost black, pasty material in which *amœbæ* were numerous. From the ileocæcal valve to the lower part of the rectum the mucosa was studded with nodular elevations which varied from about 6 millimeters to 12 millimeters in diameter and which rose about an equal distance above the level of the mucosa. In most cases the elevation was surmounted by a mass of necrotic tissue which could be scraped off, leaving a deep crater-like ulcer extending well down through the mucosa. Only one or two small, typical, irregular amœbic ulcers were observed. Many active amœbæ were found in the detritus taken from the crater-like ulcers. On section through such a nodule a red, dirty looking mass was seen extending into the submucosa and radiating for 1 cubic centimeter or more in this layer.

Microscopic examination, hæmatoxylin and eosin stain.—Lungs, alveolar septa delicate, tissue normal, very little pigment. Spleen, capsule of normal thickness; section was very cellular so that the Malpighian bodies did not stand out conspicuously. The sinuses were for the most part flattened and collapsed. The cells lining them were usually small with clear cytoplasm. There was little evidence of destruction of red blood corpuscles. The vessels, stroma and Malpighian bodies appeared normal. A few cells were found with small, dark nuclei and cytoplasm staining a coppery-red. The section of the liver showed a diffuse cloudiness and numerous areas of focal necrosis. These areas were quite extensive and often were seen to be located around the sublobular veins. In these areas the liver tissue had lost the normal staining power and the cells were opaque, red, swollen, devoid of nuclear material and either homogeneous or vacuolated. There was no evidence of reaction around the areas of focal necrosis.

Sections of the large intestines were made through several of the

nodular elevations from various parts of the large intestine. The appearances were nearly uniform in all of the cases. The mucosa between the nodules showed many crypts in which the epithelial lining was entirely converted into goblet cells. In a large number of cases the epithelium was lost entirely, leaving only the interstitial tissue. Here and there an entire crypt was converted into a granular mass, taking a deep nuclear stain. In no case were *amœbæ* found in the crypts, however. Here and there one or two adjoining crypts had become converted into granular masses and were surrounded by masses of small round cells, with numerous red blood corpuscles among them. Along either the side or the top of the elevations it was common to find that the tips of the tissue projections between the crypts were densely packed with extravasated red blood corpuscles. Close to these areas of hæmorrhage there often occurred a small bright red mass of thready fibrin mixed with detritus containing tissue cells, blood and other débris, continuous with necrotic epithelium. The necrotic mass extended as a core into the center of the nodule, in some cases reaching no further but in other cases spreading in the submucosa. Surrounding the central core of necrotic material was a dense mass of cells and red blood corpuscles, the corpuscles being often so abundant as completely to fill the tissue. Passing away from the necrotic area along the submucosa the red blood corpuscles rapidly diminished in numbers, while the cellular infiltration extended further, gradually giving way to œdema. In several places the infiltration from one nodule extended directly into that from an adjoining one. The muscular layers were practically free from involvement except along the course of the vessels where there was usually some evidence of small round-cell infiltration. A few small collections were also found in the subserosa. The cells around the necrotic mass and extending through the submucosa were for the most part lymphocytes. In many cases cells with small, densely staining nuclei were found possessing a greater amount of cytoplasm which took a slightly basic stain. Considerable numbers of cells occurred with a slightly vesicular nucleus and clear cytoplasm about two or three times the diameter of a red corpuscle in size. A moderate number of mononuclear eosinophiles were also found. These were more numerous along the outer margins of the areas of infiltration than toward the center. Great numbers of large, pale grayish, cloudy cells, evidently *amœbæ*, were found in the spaces and occasionally in the veins, especially in the advancing margin of necrosis. Often these *amœbæ* contained either blood pigment or fragments of corpuscles. In addition to the changes above noted, the connective tissue cells in the walls of some of the ulcers were swollen, with large vesicular nuclei, and there was swelling and vacuolization of the endothelial cells lining the tissue spaces and veins. In one section there was apparently a new growth of capillaries beginning near the edge of the ulcer.

In sections stained with thionin, the amœbæ failed to take the distinctive stain, but the tissue was old at the time of staining. In sections stained by Gram's method, no bacteria were found in the necrotic areas. The *amœbæ* were conspicuous in these sections. The mesenteric lymph glands showed little change in the cell nests and cell columns, except that the structure was less dense. The sinuses were moderately distended and contained many cells, (small and large mononuclears) and a few red blood corpuscles.

Anatomical diagnosis.—Amœbic dysentery; hæmorrhage into large bowel; acute anæmia; focal necrosis of liver; cloudy swelling of kidneys; ecchymoses in skin and epicardium; scar from old liver abscess. *Uncinaria and Ascaris* infection.

In this case the acute course of the disease with the abundant hæmorrhages and the peculiar nodular form of ulceration shown in the accompanying illustrations were unusual. On looking through the literature I find, however, that this lesion has been described as characteristic of the earlier stage of amœbic dysentery. Councilman and Lafleur [2] note in one case, in addition to irregular undermined ulcers, "numerous round elevations often communicating with the lesions of the bowels by a small opening. Others apparently have no opening." In their summary they speak of "sharply circumscribed projecting nodular thickenings, in which were small cavities filled with gelatinous looking pus."

The most detailed description is given by Dopter,[3] who cites an illustration of a nodule similar to one of these, and describes its development from the first stage of œdema and congestion with minute superficial erosions through a stage with elevations which he speaks of as "verrucosities" which vary from the size of a millet seed to that of a pea. He describes the false membrane and the necrosis; the destruction of entire glands and the reaction in the submucous tissues. The amount of hæmorrhage in his case was much less than in the one under discussion. He also describes the fusion of adjacent areas and a subsequent sloughing off of areas of mucosa leading to the characteristic sinus form of ulceration.

Kartulis [4] makes very little mention of such a form as the one under consideration. He describes one stage as follows: "In the case of still incomplete ulceration the plug (of necrotic tissue) is wedged in the tissue and the picture is like a furuncle with a small opening in the mucosa and the base in the submucosa." Davidson [5] refers to the occurrence of such nodules at an early stage of amœbic dysentery, and apparently a

[2] *Johns Hopkins Hosp. Rep.* (1891), II, 451.

[3] Anat. Path. Dysenterie Amibienne *Arch. de Méd. exp. et d'Anat.* Path. Paris (1907), 19, 505–541.

[4] Kolle u. Wassermann: Handbuch der pathogenen Mikroorganism, Ergänzungsband. 1907.

[5] Allbutt and Rolleston: A System of Medicine by Many Writers. London. (1907) II, Part 2, 527–542.

similar condition is briefly mentioned by Osler.[6] To those of us who saw the tissue from this case in Manila, it appeared unique but Doctor Strong believed that he had seen a similar condition before, although he does not allude to it in his article in Osler's System.[7] Jürgens[8] does not speak of finding this lesion in his experimental cats, neither is it mentioned by Ruge in Mense's Handbuch, by Manson or by Scheude. The condition in this case is certainly different from ulceration of the solitary follicles described by Jürgens and others, and in none of my sections was there evidence of special changes in the follicles.

A word as to the scar in the liver. There was no evidence of a chronic form of dysentery, neither was there evidence of peritoneal adhesions nor other evidence of previous peritonitis, yet we found the sinus leading from the puckered scar in the center of the liver to the surface. It would lead too far to speculate upon the possible relation of this scar to a previous amœbic infection, or upon the possibility of an abscess having ruptured into the peritoneal cavity without having led to the formation of adhesions.

[6] William Osler: The Principles and Practice of Medicine. New York and London. 6th ed., (1906), 2–7.

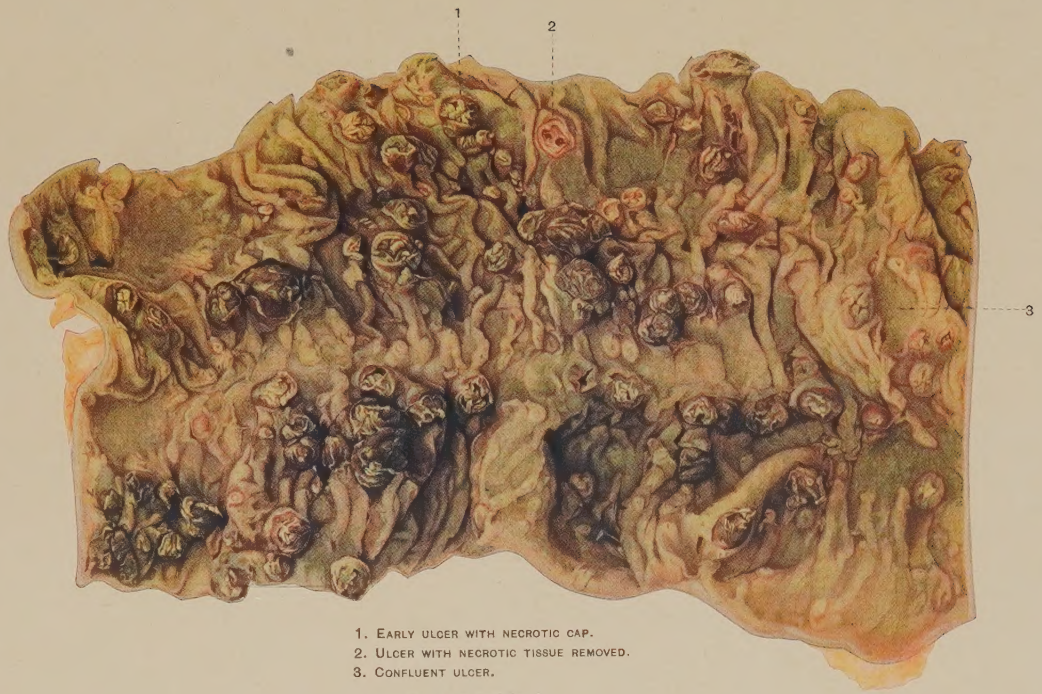
[7] Osler's system of Modern Medicine (1907), 1, 488–524.

[8] *Zrschr. f. exp. Path. u. Ther.* (1907), 4, 769–816.

ILLUSTRATION.

PLATE I.

1. Early ulcer with necrotic cap.
2. Ulcer with necrotic tissue removed.
3. Confluent ulcer.



1. EARLY ULCER WITH NECROTIC CAP.
2. ULCER WITH NECROTIC TISSUE REMOVED.
3. CONFLUENT ULCER.

PLATE I.

SIXTH INTERNATIONAL CONGRESS ON TUBERCULOSIS (HELD AT WASHINGTON, D. C., SEPTEMBER 21 TO OCTOBER 12, 1908).[1]

By Fernando Calderon and Victor G. Heiser.[2]

It was the good fortune of one of the writers to attend, as the official delegate of the United States, the First International Congress on Tuberculosis which was held at Naples, Italy, in the year 1900. The United States at that time ranked as one of the countries that had accomplished least in the combating of tuberculosis. In the eight years that have intervened between the First Congress and this, the Sixth Congress, great strides have been made along this line and the United States now ranks among the first countries that are accomplishing the most toward reducing the ravages of this disease, notwithstanding the fact that all the leading civilized countries of the world have made tremendous progress in this work from year to year.

The plan of organizing the Sixth International Congress differed from that which ordinarily prevails in Europe. The work of the different sections was characterized by a large attendance and by the earnest enthusiasm and interest which was manifest at all times. The scientific work took precedence over the social features. The latter were always arranged so as not to interfere with the real object of the congress, yet there was ample opportunity for diversion, and the wives and friends of the delegates were taken care of in a most excellent manner.

The leading authorities on tuberculosis from nearly every civilized country in the world were present, among whom might be mentioned Koch of Germany, Landouzy of France, Woodhead of England, Vladimiroff of Russia, Tendeloo of Holland, Bang of Denmark, Ishigami of Japan, Adami of Canada, von Schrotter of Austria, Calleja of Spain, and many others. Twenty-seven foreign countries were represented and the governors of many States were present in person. The daily attandance upon the scientific sessions was about 2,000, and upon popular sessions probably 5,000. A total of over 4,000 physicians registered;

[1] Read at Sixth Annual Meeting of the Philippine Islands Medical Association, February 12, 1909.

[2] Official delegates from the Philippine Islands.

some States having 200 physicians present. These figures demonstrate that this was the largest congress which has yet been held and that active interest in combating tuberculosis is rapidly increasing.

The first session was opened by the honorable the Secretary of the Treasury of the United States, and the closing session was presided over by His Excellency the President of the United States. Among other business transacted the following resolutions were passed:

Resolved, That the attention of State and central governments be called to the importance of proper laws for the obligatory notification by medical attendants, to the proper health authorities, of all cases of tuberculosis coming to their notice, and for the registration of such cases in order to enable the health authorities to put in operation adequate measures for the prevention of the disease.

Resolved, That the utmost efforts should be continued in the struggle against tuberculosis to prevent the conveyance from man to man of tuberculous infection as the most important source of the disease.

That preventive measures be continued against bovine tuberculosis, and that the possibility of the propagation of this to man be recognized.

Resolved, That we urge upon the public and upon all governments the establishment of hospitals for the treatment of advanced cases of tuberculosis.

The establishment of sanatoria for curable cases of tuberculosis.

The establishment of dispensaries and day and night camps for ambulant cases of tuberculosis which can not enter hospitals and sanatoria.

Resolved, That this Congress indorses such well-considered legislation for the regulation of factories and workshops, the abolition of premature and injurious labor of women and children, and the obtaining of sanitary dwellings as will increase the resisting power of the community to tuberculosis and other diseases.

That instruction in personal and school hygiene should be given in all schools for the professional training of teachers.

That, whenever possible, such instruction in elementary hygiene should be intrusted to properly qualified medical instructors.

That colleges and universities should be urged to establish courses in hygiene and sanitation, and also to include these subjects among their entrance requirements, in order to stimulate useful elementary instruction in the lower schools.

That this congress indorses and recommends the establishment of playgrounds as an important means of preventing tuberculosis through their influence upon health and resistance to disease.

A most noteworthy feature was the interest exhibited by those who attended the congress, and that of the press of the United States, which was characterized by its earnestness and enthusiasm.

FIRST WEEK.

The tuberculosis exhibit was pronounced by those in a position to judge to have been the most complete that has yet been assembled anywhere. Since the closing of the congress the exhibit has been transferred to New York and later it will be sent to Boston and other places. An idea of its size may be obtained when it is stated that it occupied a floor and wall space over forty times greater than that of the Marble Hall at the Ayuntamiento, Manila. The exhibit consisted mainly of models of properly

constructed dwelling houses and of small and individual shacks or tents, both in actual size and models, for the treatment of tuberculosis in different climates. These varied in style and equipment from those that cost thousands of dollars down to some which could be constructed for $25. Statistics were presented in every conceivable form. One chart showed that there had been three times as many deaths from tuberculosis in the past four years as the total number of deaths among Federals and confederates in all the battles of the Civil War. The United States Census Bureau had a red light which flashed every two minutes, each flash representing a death from tuberculosis, or 720 deaths every day in the United States alone. Cuspidors, sputum cups, and pocket flasks were shown in endless variety, together with various methods for disinfecting the same, such as burning the contents or cleansing by the use of hot water or disinfecting fluids. The exhibit from the Government Printing Office in Washington attracted much favorable comment, particularly the method by which cuspidors are carried to a special room, cleansed and disinfected without being touched by the hands. Full-sized models of dispensaries were shown by Pennsylvania and other States, illustrating the out-patient method of treating the disease. The good that may be accomplished by nurses appointed to visit the poor in their homes was well shown by the improved appearance of the houses and the disposal of the sputum of the afflicted ones in such manner as to avoid danger therefrom to others. The windows in the model houses were so arranged as to admit of perfect ventilation, painted floors were substituted for carpets, iron beds for wooden ones, and light-weight washable curtains for the heavy variety. In brief, every effort was made to show that the house should be light and well ventilated, and should contain but few things in the way of furnishing, instead of being dark and littered up with useless belongings.

The city of New York showed a series of models of city blocks. In the first series, almost the entire ground space was built over and the tuberculosis death rate was very high. The amount of unobstructed space has been increased from time to time, and a corresponding lowered death rate from tuberculosis has resulted.

The evil effects of sweeping with an ordinary broom, without first wetting the surfaces or using a special form of brush, was demonstrated by charts showing that tubercle germs have frequently been found in clouds of dust raised by the ordinary method. Many hundreds of other things too numerous to mention were also shown. The United States Department of Agriculture exhibited daily a large quantity of fresh meat which had many tuberculous lesions, which served as excellent material for demonstration. Models of traveling libraries on tuberculosis, railway cars equipped with steriopticon lantern slides, charts, etc., were shown in endless profusion.

SECOND WEEK.

The work of the second week of the congress was divided into seven sections, at which over 600 papers were read. Each section was presided over by a chairman who had an international reputation in the special field of work over which he presided, viz:

Section 1.—Pathology and bacteriology, Dr. William Welch.

Section 2.—Clinical study and therapy of tuberculosis, Dr. Vincent Bowditch.

Section 3.—Surgery and orthopedics, Dr. Charles H. Mayo.

Section 4.—Tuberculosis in children, Dr. Abraham Jacobi.

Section 5.—Hygiene, social, industrial, and economic aspects of tuberculosis, Edward T. Devine.

Section 6.—State and municipal control of tuberculosis, Dr. Walter Wyman.

Section 7.—Tuberculosis in animals and its relation to man, Dr. Leonard Pearson.

All sections met daily from 9 to 12 and from 2 to 5, and at times two sections held combined meetings to discuss questions of common interest; a general meeting of all sections was also held every night, beginning at 8 p. m.

Under the section entitled "The State and municipal control of tuberculosis," the papers were read which were deemed to be of the most practical interest to the Philippine Islands, and, consequently, the greater portion of our time was devoted to this section.

On September 29, Doctor Heiser read a paper entitled "The tuberculosis problem in the Philippines and the elimination of intestinal parasites as the first step in its solution." On October 1, Doctor Calderon read a paper entitled "Notes on tuberculosis in the Philippines."

The scientific work of the congress showed clearly that remarkable unanimity prevailed among the delegates upon the following points:

1. That tuberculosis in its early stages is a curable disease.

2. That it is a house disease; that is to say, that people who live an outdoor life are not afflicted with tuberculosis, and the more confined the living quarters are the more prevalent is the disease.

3. That it is a simple and practicable matter to avoid contracting tuberculosis by introducing large volumes of air into the house, night and day, winter and summer, or, better, by sleeping out of doors altogether.

4. That among the best ways to cure tuberculosis is to live an outdoor life, regardless of what the climate may be, with only such exercise as a physician prescribes and a good, simple diet which should consist mainly of eggs and milk.

6. That the successful treatment of the disease is not necessarily confined to specially favored localities, but that many cures may be effected in almost any climate or locality.

THIRD WEEK.

The third week of the congress was devoted to a continuation of the exhibition, lantern demonstration, lectures, and visits to Baltimore and the near-by places at which tubercular sanatoria are located.

OFFICIAL VISITS.

Philadelphia, White Haven, Saranac, Boston, and New York were visited for the purpose of observing the dispensary and hospital work in large cities as well as the manner in which the different kind of sanatoria are conducted. After carefully inquiring into and seeing the foregoing, it is again plainly evident that the authorities are practically unanimous in their methods of combating tuberculosis, the principal difference being to suit them to the financial abilities of the different communities in which they were in force.

The measures readily divide themselves into the following:

1. Registration and classification of cases.
2. Popular lectures on tuberculosis and popular articles in the press.
3. Treatment of tuberculosis by the dispensary system.
4. Confining the hopeless cases in separate hospitals located in the city.
5. Sending early cases to a sanatorium in the country.

TUBERCULOSIS WORK IN PENNSYLVANIA.

As practically all the States are endeavoring to adopt the systems in use in Pennsylvania, Maryland, New York, and Massachusetts, the one now used in Pennsylvania is hereby briefly outlined:

1. The collection and tabulation of statistics relating to tuberculosis, through official morbidity and mortality reports of each individual case.
2. The establishment of one or more sanatoria for the treatment of incipient cases, including infirmaries for advanced and hopeless cases.
3. The establishment of dispensaries in each county of the State for the care of cases which can not avail themselves of sanatorium treatment, including home visitations and the study of occupational conditions.
4. The maintenance of pathological laboratories for the free examination of sputum and tuberculous lesions, and biological laboratories for the possible development of immunitive and curative products.
5. The restriction of tuberculosis by the disinfection of rooms, buildings (private and public), conveyances, and carriers, and by supervision and regulation over the general avenues of infection.
6. The dissemination of knowledge relative to the communicability, care, and prevention of tuberculosis.

The last session of the Pennsylvania legislature appropriated $1,000,000, United States currency, for the continuation of the fight against tuberculosis in that State. The sums raised from private effort probably amounted to as much again. Dr. Lawrence Flick, the eminent authority on tuberculosis, estimates that as a result of this appropriation at least 5,000 lives are already saved annually in Pennsylvania alone.

DISPENSARIES.

One of the principal weapons with which to combat tuberculosis in large cities is the use of the outdoor dispensary, at which no other disease except tuberculosis is treated. Pennsylvania has established

such a dispensary in every county seat in the State and in some of the principal cities. These, as well as those being built by the munificence of Mr. Phipps, are perhaps typical of their class. They consist usually of two rooms, one a waiting room where the patients are received by the nurse, who records the history and makes a most complete card index record of the case; temperatures are taken, and in general the patient is in every way prepared for the doctor's visit. The latter usually arrives after the patients have been prepared for him, makes the diagnosis and prescribes the treatment.

These dispensaries are usually open from 8 until 1 each day and have, as a rule, one nurse and two physicians on duty. In addition to the nurse who is on duty in the dispensary, there are usually two who make visits to homes of tuberculosis patients, and give them practical demonstration in hygienic living. They also recommend as to whether fresh eggs and milk should be supplied gratis.

SANATORIUMS AND CAMPS.

White Haven.—This institution differs from all of the others visited in that a systematic trial is being made on a large scale to put the sanatorium on a self-supporting basis by means of the labor of the patients. So far as our own observations went, it can not be said that this plan has proved successful up to this time.

Trudeau's.—As is well known, the oldest advocate of the outdoor treatment of tuberculosis is Doctor Trudeau, and it is here that it is most interesting to observe the gradual development of small buildings suitable for the treatment of tuberculosis. The first primitive shack still stands and each structure built since is an improvement on its predecessor. The accompanying illustrations (figs. 1 and 2) show what he regards to be the most modern type of building for the outdoor treatment of tuberculosis. Doctor Trudeau's place is situated in the Adirondacks at Saranac Lake.

Ray Brook.—The State of New York has erected at Ray Brook a large brick structure much on the order of a modern hospital building, where patients are treated in wards of the two-story type, with enormous air space allowance for each patient. In addition, a few tents or shacks are built near by for the treatment of such cases as are considered more favorable for the hardy outdoor life.

Beelitz, Germany.—At Beelitz, Germany, there is probably one of the most modern tuberculosis sanatoriums in the world. This was built by a German Life Insurance Company for the use of their policy holders. The institution is built upon the same general lines as the Ray Brook institution mentioned above, but on account of the greater amount of funds available, the institution presents a more finished character.

NIGHT AND DAY CAMPS.

At Pittsburg, Pa., and Boston, Mass., there exist on the outskirts of the city large day camps where persons suffering with incipient tuberculosis are encouraged to go during the day time, and are given lessons in hygiene and furnished with wholesome diet, free of charge. It is now proposed to change these camps to night camps so that persons may sleep there, and, in suitable instances, go to their business during the day time.

TREATMENT.

It was the overwhelming opinion of those actively engaged in the treatment of tuberculosis that the use of tuberculin and serums is largely in the experimental stage, that its general use at the present time is not justified, and that the subject has scarcely passed out of the laboratory stage. There was a unanimous opinion, however, that the best method of combating tuberculosis was by the free administration of eggs and milk, and, occasionally, a tonic. Practically no other treatment is given. All persons interviewed also emphatically expressed the opinion that the success depended upon the early diagnosis of the disease. In this connection, it might be well to mention that beds in sanatoriums for incipient cases were scarcely ever found to be filled. Statistics show that 55 per cent of the early cases recover, while only 11 per cent of the more advanced cases recover. It is also generally believed that cold weather has the most beneficial influence. This is based on the fact that cases invariably do better in the winter time than in the summer. Considerable stress was also laid upon the fact that in the past it has been customary to allow too much exercise, and there seems to be little question but that harm has often followed overexertion.

COST OF TUBERCULOSIS.

Professor Fisher, of Yale University, estimates the death rate from tuberculosis in all its forms in the United States to be 164 per 100,000 of population, and the number of deaths in 1906 at 138,000. At this rate, 5,000,000 people now living in the United States will die of tuberculosis. The average age at death for males is 37.6 years; for females, 33.4 years. The "expectation of life" lost (though estimated on a specially high mortality rate) is at least 24 years, of which at least 17 fall in the working period. The average period of disability preceding death from tuberculosis exceeds three years, of which the latter half is a period of total disability.

The money cost of tuberculosis, including capitalized earning power lost by deaths, exceeds $8,000 per death. The total cost in the United States exceeds $1,000,000,000 per annum. Of this cost about two-fifths, or over $440,000,000 per annum, falls on others than the consumptive.

An effort to reduce the mortality by one-fourth would be worth, if necessary, an investment of $5,500,000,000. The cost of treating patients at sanatoria is repaid many times over in lengthened working lives. The erection of isolation hospitals for tuberculosis is probably the most profitable method at present of reducing the cost of tuberculosis.

Upon the above bases there are 25,000 deaths or more per year in the Philippines.

RECOMMENDATIONS.

1. That the compulsory registration of cases of pulmonary tuberculosis be put into effect immediately, at least in the city of Manila.

2. That one or more dispensaries solely for the outpatient treatment of tuberculosis be opened in Manila, to which one or more nurses be attached for the purpose of visiting patients in their homes. Also that provision be made for the microscopical examination of sputa.

3. That the necessary funds be provided for a trial of the "open-air method" in Benguet or some other place where an equally low temperature may be had, for the treatment of not to exceed twelve tubercular patients.

4. That provision be made on an elevated site near Manila for treating a limited number of incipient cases of tuberculosis, for a period of not to exceed three months each, by requiring their presence only during the night in order that the advantages of the open air method, the disposal of sputa, and the precautions to be taken to avoid transmitting the infection to others may be demonstrated.

5. That in order to furnish a practical object lesson, sanitary cuspidors be provided and used in all public buildings, including public schools, and that the sweeping or cleaning of such buildings be done in such manner as to prevent the formation of clouds of dust.

6. That the public streets be swept only when in a wet condition, so as to avoid the unnecessary blowing about of dust. In this connection, it is suggested that the cleansing of streets by flushing, as is now done in Cincinati and other cities of the United States, be thoroughly investigated with the view of discontinuing street sprinkling and sweeping in Manila.

7. That arrangements be made for supplying the public press with information relative to tuberculosis.

8. That instruction on tuberculosis be continued in the public schools and begun in all other schools where it is not taught at present.

9. That in communities where hookworms prevail, steps be taken to eradicate them, because the lowered vitality which they induce predisposes strongly to tuberculosis.

10. That as many of the above recommendations as possible be put in force in the provinces.

ILLUSTRATIONS.

FIG. 1. Plan of cottage for the Adirondack Cottage Sanatorium, Saranac Lake, New York. Front elevation.
2. Floor plan of same cottage.

FIG. 1.—FRONT ELEVATION.

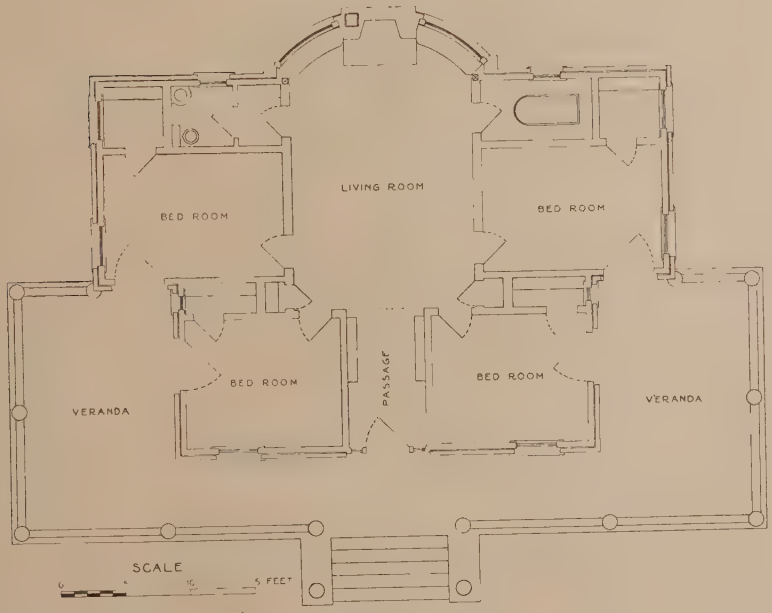


FIG. 2.—FLOOR PLAN.

COTTAGE FOR THE ADIRONDACK COTTAGE SANATORIUM, SARANAC LAKE, NEW YORK.

THE CUTANEOUS REACTION IN LEPROSY. PRELIMINARY REPORT.[1]

By Oscar Teague.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

One of the greatest advances made in the study of immunity during the past two years has been the recognition and investigation of a condition which is in a sense the opposite of immunity, namely a condition of hypersensitiveness. It has been known for a long time that when an animal is injected with certain toxic substances, it may react and produce antibodies which render it more resistant to the toxin in question; but it is only recently that marked attention has been given the fact that under certain circumstances an animal may react and become more suspectible to the substance injected. The hypersentitivenes of the guinea pig to injections of horse serum has been carefully studied and will illustrate the point in question A normal guinea pig may be given 5 or 6 cubic centimeters of horse serum subcutaneosly or intraperitoneally without showing any abnormal symptoms. But if a guinea pig be given one-tenth of a cubic centimeter of horse serum and, after a period of ten days or more has elapsed, 5 cubic centimeters of horse serum are administered intraperitoneally, the animal, after a few minutes, shows signs of restlessness, then falls over on its side, struggles convulsively and dies of respiratory failure. The first injection of a minute quantity of horse serum has "sensitized" the guinea pig so that horse serum is now extremely toxic for it. If the second injection had been given within the ten-day interval, the guinea pig would not have been affected. This incubation period of the hypersensitive reaction has lead some investigators to believe that the process depends upon the formation of antibodies here just as in the case of the immunity reactions. The hypersensitiveness when once established has been shown to last a year and even longer, and probably is present as long as the animal lives.

Instead of horse serum, probably almost any other foreign protein could be used to call forth hypersensitiveness, and this has been already demonstrated for egg white, proteins from certain plants, bacterial extracts and other substances.

The study of the immunity reactions brought forth abundant fruit for the practical side of medicine in the discovery of diphtheria and

[1] Read before the Manila Medical Society on September 8, 1908.

tetanus antitoxin, in the Widal and precipitin tests, in vaccine therapy, etc. Likewise, the study of the hypersensitive reaction, though still in its infancy, has already demonstrated that the rare instances of sudden death following the injection of antitoxin and the rashes, joint pains and fever occurring during the course of serum treatment, are in no wise due to the antitoxin as such but to the vehicle of the antitoxin and are hence nothing more or less than the expression of the hypersensitive reaction to the proteins of the horse serum.

Another important acquisition to practical medicine resulting from the study of hypersensitiveness, is von Pirquet's cutaneous reaction which was first announced in May, 1907. Von Pirquet had observed that if the skin of a tuberculous patient was scarified and moistened with a drop of Koch's old tuberculin, within from twelve to forty-eight hours an urticaria-like swelling or a papule surrounded by a reddened area appeared. His technique consisted in placing a drop of old tuberculin on the skin of the forearm which had been previously cleansed with ether and in scraping away a small portion of epidermis beneath the drop by a boring motion with the point of a scalpel. A bit of cotton was then placed in the tuberculin and left for ten minutes. Instead of a scalpel he later used a special instrument with a chisel-like point for removing the epidermis. Others have made a short superficial incision with a sharp knife, care being taken not to draw blood. A control scarification without tuberculin is made on the same arm for comparison. In the case of a positive reaction a slight reddening appears in about twelve hours and the swelling and redness reaches its maximum in from twenty-four to forty-eight hours lasting four or five days or longer; whereas the swelling due to a slight mechanical injury disappears in a day or two.

Very soon after von Pirquet made known the discovery of his cutaneous reaction, both Wolff-Eisner and Calmette announced results obtained by dropping a diluted tuberculin into the conjunctival sack of tuberculous patients. The reaction that follows this procedure has become known as the ophthalmoreaction, though in reality it is a conjunctival reaction and the eye itself is in no way concerned. Calmette thought that the glycerine of the old tuberculin was irritating and hence precipitated the tuberculin with alcohol, and dissolved the precipitate in water. However, later workers have found that in the dilutions in which it is used (one-half to 1 per cent), the old tuberculin is entirely satisfactory.

Another modification of the skin reaction was suggested by Moro,[2] who prepared an ointment of equal parts of lanolin and old tuberculin and simply rubbed it into the skin over an area about 5 centimeters in diameter. The positive reaction was indicated by the appearance of papules and vesicles in the treated area.

[2] *Münch. med. Woc.* (1908), **55-1**, 216.

The important question to be answered in regard to these reactions is what value have they in the diagnosis of tuberculosis. A rather voluminous literature has already appeared with this object in view, which is not surprising when one considers the ease with which the tests may be applied and that every hospital offers material for investigating one phase or another of the question.

The consensus of opinion with regard to von Pirquet's cutaneous reaction seems to be that it is a specific reaction for tuberculosis and hence scientifically and statistically valuable. As an aid to diagnosis, a distinction must be made according as children or adults are being subjected to the test. In children, a positive result indicates that the child is tuberculous but a negative one does not necessarily mean that the child is free from tuberculosis since only about 50 per cent of the cases of miliary tuberculosis and tuberculous meningitis give the reaction. The test is of distinct value as an aid in diagnosis in children. In adults, since from 50 to 90 per cent of healthy individuals react positively, only the failure to get the reaction can be of service, and its diagnostic value is extremely limited.

Wolff-Eisner's conjunctival reaction yields approximately the same results as the cutaneous reaction, though he claims that it does not indicate healed foci as does the cutaneous reaction and that therefore it is of more value as an aid to diagnosis in adults.

The ointment reaction of Moro would seem to give less satisfactory results than the other two.

It will be remembered that the old subcutaneous injection of Koch's tuberculin was open to the same objections as are encountered in these recent methods: that is, it called forth a reaction in a large percentage of healthy adults and failed to give the reaction in many cases of miliary tuberculosis, tuberculous meningitis and in cachectic individuals.

If the cutaneous and ophthalmo-reactions should prove to be of equal diagnostic value with Koch's subcutaneous injection, then the latter method would probably cease to be used for diagnostic purposes because (1) of the danger of activating an old tuberculous focus, (2) it can not be used in patients with fever, (3) it requires that the patient be kept in bed four days, two days for observation before the injection and two days after the injection.

Attempts have been made to apply the cutaneous and ophthalmo tests to a number of other bacterial diseases. Chantemesse's work on the conjunctival reaction in typhoid fever attracted wide attention, but has not been confirmed by German investigators. However, Meroni [3] recently has obtained positive results on 25 cases with more than that number of controls.

[3] *Münch. med. Woc.* (1908), **55-I**, 1379.

Link [4] used the cutaneous reaction on 14 cases of typhoid and paratyphoid fever. Killed cultures of *Bacillus coli communis, typhosus* and *paratyphosus* were prepared and all three suspensions used on all the patients. One case in which paratyphoid bacilli had been found in the stool some months previously and in which the serum of the patient gave a negative Widal reaction to all three organisms, showed a distinct cutaneous reaction to *Bacillus paratyphosus* and no reaction to *Bacillus coli communis* or *Bacillus typhosus.* In general the reactions agreed with the agglutination tests but taken all in all they were rather unsatisfactory. He suggests that it would be interesting to see if typhoid carriers give the reaction. If this should prove to be the case the reaction would be of value in locating such dangerous individuals in the army and among other large bodies of men who live in close contact with one another.

In glanders the ophthalmo-reaction has given good results with horses and Martel [5] has reported four human cases which gave positive reactions with mallein diluted one-tenth.

Attempts, in most instances unsuccessful, have been made to distinguish between infection with the bovine and with the human type of the tubercle bacillus by vaccinating simultaneously with the two kinds of tuberculins, but the patients react to both. Wolff-Eisner has suggested that by working quantitatively; i. e., by using decreasing dilutions of the two tuberculins and comparing the degree of the resulting reactions better results might perhaps be obtained.

The reaction has been tried in diphtheria with doubtful results.

In April, 1907, Wooley [6] suggested that, since the leprosy bacillus has not been grown on culture media, nodules obtained from a leprous patient be extracted in salt solution and the resulting extract be used as a vaccine for treatment of the patient. It was but a short step to use such an extract in an attempt to obtain a cutaneous reaction in lepers such as von Pirquet had observed in tuberculosis. I hoped that in this way an aid in the diagnosis of doubtful cases of leprosy might be obtained.

Since the leprosy bacillus bears more resemblance to the tubercle bacillus than to other pathogenic organisms, extracts were prepared in a similar way as in the preparation of old tuberculin.

Four different extracts were made as follows: first, from nodules taken from living lepers, second, from the nodulous skin of a dead leper, third, from the spleen of a dead leper, fourth, a control from the skin of a cholera corpse. The material thus obtained was cut into small pieces or ground in a mortar in case of the spleen, and extracted in 5 per cent glycerine. It was then heated on the water bath until the volume was reduced to about one-tenth of the original.

[4] *Loc. cit.* (1908), **55-I**, 730.
[5] Berl. klin. Woch. (1908), **45**, 451.
[6] *Proc. Soc. Exp. Med. & Biol.* N. Y. (1907), **4**, 121.

Fifty lepers were vaccinated with these extracts, a control vaccination with the extract of skin from the cholera case being made in each instance. In two or three cases there was a doubtful reaction, but otherwise the vaccinations were in all respects like the controls. Further attempts will be made to secure a more concentrated extract of the leprosy bacilli. Owing to the low resistance of the tissues of lepers, it was not thought advisable to use the ophthalmo-reaction until the cutaneous reaction had been given a thorough trial.

I wish to thank Doctor Newberne for the courtesies extended to me at the San Lazaro Leper Hospital.

THE NASTIN TREATMENT OF LEPROSY.[1]

By Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

In 1904 Deycke Pasche and Reschad Bey[2] of the Imperial Hospital and Medical School of Constantinople, while attempting to cultivate the leprosy bacillus, obtained a streptothrix in pure culture to which they gave the name *Streptothrix leproides*. The culture was made by laying back a flap of skin containing a leprous nodule and excising a piece of tissue from the under surface of the flap. The tissue was placed in salt solution and kept at incubator temperature. After three weeks the filaments of the streptothrix were seen growing from the tissue in great profusion.

With the idea of determining whether or not this streptothrix bore any relationship to the leprosy bacillus, the living culture was injected subcutaneously in a very severe case of leprosy. Strange to say, this patient showed marked improvement in his subjective symptoms and requested that the treatment be continued. Accordingly injections were given at seven-day intervals and after two months the patient considered himself cured and left the hospital. Similar results were obtained in three other cases.

The streptothrix was then grown in large quantities and the protein substances of the culture separated from the fats by extraction with ether. On injecting these two portions separately into patients, the authors came to the conclusion that the etherial extract contained the curative agent. Finally they believed that they had isolated this active principle and that it was a true fat—a glyceride of one of the higher fatty acids. To this fat they gave the name "nastin." The authors claimed that subcutaneous injections of this substance produced a specific action on leprous nodules, causing inflammation with subsequent softening. This reaction was sometimes accompanied by high fever lasting for days.

[1] Read at the Sixth Annual Meeting of the Philippine Medical Association, Manila, P. I., February 11, 1909.

[2] *Deutsche med. Wchnsch.* (1905), **31**, 488.

The hypothesis advanced to explain this action was as follows: The leprosy bacilli contain the same fat as "nastin," or a similar one, and it is to this fat that the bacilli owe their resistance to the protective forces of the body. By spaced injections with nastin an active immunity is produced against the resistant fatty substance of the bacilli, so that these latter are destroyed.

This hypothesis is not in accord with our ideas with regard to immunity; for with the exception of the glucosides of Ford of Johns Hopkins University, immunization has not been produced with a substance known to be of non-protein nature. It is, to say the least, highly improbable that immunization could be effected against a chemically pure fat. In his lecture [3] delivered at the London School of Tropical Medicine, Professor Deycke makes no further mention of this hypothesis but advances another one to explain the destruction of the leprosy bacilli by the Nastin treatment. He had found that benzoyl chloride dissolves out the fatty substances from tubercle bacilli much more readily than the ordinary fat solvents, such as ether and chloroform. On mixing benzoyl chloride with his Nastin he obtained much more constant reactions than with the Nastin alone. The nastin now on the market consists of such a mixture in the proportions which he found to yield the best results. He believes—to use his own words—that—

"The nastin is carried to the leprosy bacilli, to which, owing to its near chemical and physical relation, it attaches itself, and then benzoyl can fully display its anti-bacterial action in the fat-removing sense. When deprived of fat the leprosy bacilli seem to be doomed; the human organism then effects with comparative ease the further dissolution and ultimately the complete destruction of the bacterial nuclei."

Although we did not agree with Professor Deycke's theoretical considerations, nevertheless in view of the favorable results reported by him, at Doctor Strong's suggestion I determined to give the method a trial. Four patients were selected at San Lazaro Hospital. Two were well-marked cases of the nodular type in young boys of ten years, both free from ulcerations; the other two were male patients of about twenty years of age, one with very slight lesions in which only comparatively few leprosy bacilli were found; the other was a well-marked case having both nodules and ulcers.

The injections were begun on the 8th of September, 1908, and have been continued up to the present time, being given at about seven-day intervals except for two slight interruptions due to delay in receiving the nastin from Europe.

A general febrile reaction was observed only once and then in one of the well-marked cases. About twenty-four hours after the fifth injection

[3] *Brit. Med. Journ.* (1908), I, 802.

the patient had a temperature of 104° and complained of a severe headache and general malaise. The fever lasted about twenty-four hours and then all unusual symptoms quickly disappeared. In this same patient some of the nodules have become soft and have broken open, the ulcers thus formed healing readily.

However, since the febrile reactions and healing of nodules sometimes occur without any treatment whatsoever in severe cases of leprosy, and especially since none of the other patients under treatment have shown similar reactions, we do not feel inclined to look upon the nastin injections as the cause of the phenomena in this case. Furthermore, in spite of the fact that a few isolated nodules have healed, it can not be said that there is any noticeable improvement in the patient.

Professor Deycke states that—

"We will be able, except in the most severe, hopeless cases, to effect at least the arrest of the leprous process; frequently, however, far better results will be obtained."

Some of his results were obtained within two months after treatment was begun; in other instances the patients were under treatment for over twelve months. I regret that the cases here considered have been under treatment for only five months but one would have a right I believe, to expect some improvement in them in this time, judging from Professor Deycke's reports.

Two other patients who were under X-ray treatment received at their own request the nastin treatment also. One of these, a rather mild case of the nodular type who, however, has been under treatment for a shorter time than the other patients, recently developed a fresh crop of nodules. I mention this because Professor Deycke states that the nastin is able to hold all but the very severe cases in check although it can not cure all of them.

In conclusion, then—

(1) It seems to us unlikely that the *Streptothrix leproides* of Professor Deycke bears any relationship to the leprosy bacillus;

(2) The nastin treatment is not based upon any of the established principles of immunity reactions; it is not a vaccine therapy, but is a drug treatment and is purely empirical; it is claimed that nastin is a glyceride of one of the higher fatty acids and in this connection it is interesting to note that Chaulmoogra oil, one of the most widely known drugs employed for leprosy, is also a fatty substance;

(3) The nastin treatment has not produced beneficial results in the four cases which I have treated during the past five months.

FILTRATION OF IMMUNE SERUMS.

By E. H. Ruediger.

(From the Serum Section, Biological Laboratory, Bureau of Science, Manila, P. I.)

Because of the difficulties encountered in endeavoring to obtain antiserums for therapeutic purposes free from corpuscles, precipitates, and bacteria, it was thought advisable to study the effects of filtration through Berkefeld filters on immune serums. Early in the year 1906 attempts to filter anticattle plague serum had been made in this laboratory, but were soon abandoned because the filters invariably became clogged.

More recently filtration of serum was again attempted and it was found that the serum readily passes through the filter, provided that it is free from blood corpuscles, precipitates and other extraneous matter. These substances as a rule are removed easily from the serum by centrifugating for thirty minutes at a speed of 3,000 revolutions per minute, and at the present time all serums prepared by this laboratory are passed through a germ-proof filter prior to bottling. The serum thus obtained is perfectly clear and is free from bacteria which may have entered accidently during the process of handling.

TECHNIQUE.

The serum, having been collected, is centrifugated at a speed of 3,000 revolutions per minute for thirty minutes, which process usually renders it fairly clear. It is now passed through a clean, sterile Berkefeld filter marked N or W. If, after centrifugating, the serum is not clear, it is advisable to first pass it through a Berkefeld V filter to remove most of the extraneous matter which might lead to rapid clogging of the finer grained filter marked N or W. Using an apparatus of one liter capacity, one liter of serum under two atmospheres pressure should pass through the Berkefeld filter V in three minutes or even in less time, while with the N filter not more than five minutes should be required. A ten-liter filtering apparatus should deliver a liter of serum through Berkefeld V filter in one minute, and not more than three minutes per liter should be required when an N filter is used.

Care must be taken to cleanse the filter after it has been used. Any serum left in the pores of the filter will be coagulated by autoclaving and

render the filter impermeable. To insure thorough cleansing, the following procedure has been found satisfactory: immediately after having been used, the surface of the filter is scrubbed with a brush under running water and the serum is removed from the pores of the filter by passing through it a liter or more of distilled water or an aqueous solution of 0.75 per cent sodium chloride. The filter is then boiled in distilled water, and after the boiling, is again washed by passing water through it. It has been my experience that if the boiling is omitted the filter gradually becomes impermeable, and to insure a thorough cleansing none of the steps mentioned should be omitted.

Martini,[1] in studying the effect of filtration on antidiphtheritic serum, demonstrated great loss in the potency of the serum after it had passed through Chamberland filters. Serum which before filtering contained 140 units of antitoxin per cubic centimeter, after filtering contained 100 units per cubic centimeter. Another lot of serum which contained 135 units of antitoxin per cubic centimeter, lost 75 units per cubic centimeter through filtering. By evaporating he reduced antidiphtheritic serum to the consistency of syrup; the concentrated serum contained 850 units of antitoxin per cubic centimeter; after passing it through a Chamberland filter it contained only 40 units of antitoxin per cubic centimeter, having lost 810 units per cubic centimeter.

Dziergowsky[2] passed antidiphthetric serum through Chamberland filters and could not demonstrate any loss of antitoxin thereby.

Cobbet[3] repeated the work of the previous authors and showed that antidiphtheritic serum may be passed through Chamberland filters without losing its potency provided the filters are clean and the serum passes through readily. On the other hand, if a filter is allowed to clog, the serum passing through drop by drop invariably suffers great loss of antitoxin.

I have studied the question as to whether a serum suffers any loss in immunizing value by being passed through Berkefeld filters. The following experiments show the immunizing value of unfiltered and filtered antitetanic and antidiphtheritic serums and the agglutinating value of unfiltered and filtered typhoid serum.

EXPERIMENT NO. I.

A quantity of about 1,500 cubic centimeters of antitetanic serum was divided into four portions A, V, N and W. Portion A was neither centrifugated nor filtered, portion V was passed through Berkefeld filter V, portion N was passed through Berkefeld filter N and portion W was passed through Berkefeld filter marked W.

[1] *Centralb. f. Bakt. etc.* (1896), **20**, 796.
[2] *Ibid.* (1897), **21**, 333.
[3] *Ibid.* (1898), **24**, 386.

Varying quantities of each of these portions were mixed with 100 lethal doses of tetanus toxin, allowed to stand in a test tube for thirty minutes and were then injected under the skin of guinea pigs weighing between 245 and 255 grams.

TABLE I.—*Unfiltered and filtered antitetanic serum mixed with tetanus toxin and tested on guinea pigs.*

Portion of serum.	Quantity of—		Result.
	Serum.	Toxin.	
	cc.	*Lethal doses.*	
A	1/100	100	Lived.
	1/1000	100	Lived.
	1/1200	100	Died.
	1/1400	100	Died.
V	1/100	100	Lived.
	1/1000	100	Lived.
	1/1200	100	Died.
	1/1400	100	Died.
N	1/100	100	Lived.
	1/1000	100	Lived.
	1/1200	100	Died.
	1/1400	100	Died.
W	1/100	100	Lived.
	1/1000	100	Died.
	1/1200	100	Died.
	1/1400	100	Died.

As is shown by the Table I the neutralizing values of these portions of the serum must be considered identical. Although 0.001 cubic centimeter of portion W did not protect the guinea pig inoculated, such variations are entirely within the bounds of experimental error and even greater differences are frequently encountered with one and the same serum. Portions N and W were sterile.

EXPERIMENT NO. II.

To 200 cubic centimeters of antitetanic serum 800 cubic centimeters of physiological salt solution was added. This diluted serum was divided into four portions, A, V, N and W. Portion A remained unfiltered, and portions V, N and W were passed through the Berkefeld filters so lettered.

Varying quantities of these portions of serum were mixed with 100 lethal doses of tetanus toxin, allowed to stand for thirty minutes and were then injected under the skin of guinea pigs weighing between 245 and 255 grams.

TABLE II.—*Antitetanic serum diluted with physiological salt solution in proportion of 1–4, unfiltered and filtered tested on guinea pigs.*

Portion of serum.	Quantity of—		Results.
	Diluted serum.	Toxin.	
	cc.	*Lethal doses.*	
A	1/80	100	Lived.
	2/80	100	Lived.
	2 1/2 0	100	Died.
	2 2/8 0	100	Died.
V	1 3/8 0	100	Lived.
	2/80	100	Lived.
	2 1/8 0	100	Died.
	2 2/8 0	100	Died.
N	1/80	100	Lived.
	2/80	100	Died.
	2 1/8 0	100	Lived.
	2 2/8 0	100	Died.
W	1/80	100	Lived.
	2/80	100	Lived.
	2 1/8 0	100	Died.
	2 2/8 0	100	Died.

The results obtained shown in Table II show the neutralizing value of the filtered serum to be practically identical with that of the unfiltered serum.

Bacteriological examination showed portions N and W free from bacteria.

EXPERIMENT NO. III.

A quantity of antidiptheritic serum was divided into four portions A, V, N and W. Portion A was not filtered while portions V, N and W were passed through Berkefeld filters V, N and W respectively.

Varying quantities of these different portions were mixed with a test dose of diphtheria toxin, allowed to stand for thirty minutes and were injected under the skin of guinea pigs weighing between 245 and 255 grams.

TABLE III.—*Antidiphtheric serum unfiltered and filtered mixed with diphtheria toxin and tested on guinea pigs.*

Portion of serum.	Quantity of—		Results.
	Serum.	Toxin.	
	cc.		
A	$\frac{2}{100}$	Test dose	Lived.
	$\frac{1}{100}$	Test dose	Lived.
	$\frac{3}{100}$	Test dose	Died.
	$\frac{1}{100}$	Test dose	Died.
V	$\frac{2}{100}$	Test dose	Lived.
	$\frac{1}{100}$	Test dose	Lived.
	$\frac{3}{100}$	Test dose	Died.
	$\frac{1}{100}$	Test dose	Died.
N	$\frac{2}{100}$	Test dose	Lived.
	$\frac{1}{100}$	Test dose	Lived.
	$\frac{3}{100}$	Test dose	Died.
	$\frac{1}{100}$	Test dose	Died.
W	$\frac{2}{100}$	Test dose	Lived.
	$\frac{1}{100}$	Test dose	Lived.
	$\frac{3}{100}$	Test dose	Died.
	$\frac{1}{100}$	Test dose	Died.

The results shown in Table III would suggest a loss of antitoxin in portion W, but owing to the small number of animals used a definite statement can not be made.

A few cubic centimeters of filtrates N and W planted in agar yielded no bacterial growth.

EXPERIMENT NO. IV.

A quantity of typhoid agglutinating serum was divided into four portions A, V, N and W. Portion A remained unfiltered, and portions V, N and W were passed through the corresponding Berkefeld filters. After filtration of portions V, N and W the agglutinating values of the different portions were determined on a suspension of Bacillus typhosus.

TABLE IV.—*Typhoid agglutinating serum unfiltered A, and filtered V, N and W tested for its agglutinating value.*

Dilution.	Portion.				Time.
	A.	V.	N.	W.	
					Hours.
1–100	+	+	+	+	9
1–200	+	+	+	+	9
1–400	+	+	+	+	9
1–800	+	+	+	+	9
1–1,000	+	+	+	+	9
1–1,400	+	+	+	+	9
1–1,800	+	+	+	+	9
1–2,200	+	+	+	+	9
1–2,600	—	+	—	—	9
1–3,000	—	—	—	—	9
1–3,200	—	—	—	—	9
1–6,400					9

A glance at Table IV shows the agglutinating value of the filtered portions V, N and W to be practically identical with that of the unfiltered portion A.

EXPERIMENT V.

The influence of high pressure on the permeability of Berkefeld filters to small yet microscopically visible bacteria.

It has been known that bacteria which are not ultramicroscopic may and will pass through the pores of Berkefeld filters. Wherry[4], in the year 1902, showed that the bacillus of guinea pig pneumonia frequently passes through the Berkefeld filters under ordinary conditions of filtration.

In this laboratory, the Berkefeld filter marked W is used almost exclusively for the final filtration of anticattle plague serum. Filtration was formerly carried on with the Chamberland filter stand under a pressure of one and one-half to two atmospheres; bacterial contamination of the filtrate was rare, but the filtration frequently was slow and tedious. In order to facilitate the filtration the air pressure in the institution, which is kept fairly constant by an automatic electric regulating device, was increased to four atmospheres. Bacterial contamination of the filtrate soon became common and the contaminating organism usually was a small bacillus. This at once led me to study the influence of various pressure on the permeability of the filters to these bacilli.

Method of investigation.—Nine new Berkefeld filters, three marked V and designated here as V_I, V_{II}, and V_{III}, three marked N, designated N_I, N_{II}, and N_{III}, and three marked W designated W_I, W_{II} and W_{III}

[4] *Journ. Med. Research* (1902) **8**, 322.

respectively, were washed by passing distilled water through them and were sterilized in the autoclave.

Three hundred cubic centimeters of previously filtered serum inoculated with these small bacilli were passed through each of the nine sterile filters under various pressures ranging from one to four atmospheres; the portions of the serum were then collected in a sterile receptacle provided with a protected mouthpiece and stopcock at the bottom, and then bottled in two portions, *a* and *b*, of about 150 cubic centimeters each. Portion *a* was drawn off into a sterile bottle as soon as about 150 cubic centimeters had collected, and portion *b* was bottled after all serum including the froth obtained in the end had passed through the filter.

After two days' incubation 1 cubic centimeter of each portion of the filtrate was planted in liquefied agar.

TABLE V.

Filter.	Portion.	Pressure.			
		1 atmosphere.	2 atmospheres.	3 atmospheres.	4 atmospheres.
V I	a	+	+	+	+
	b				
V II	a	+	+	+	+
	b	+	+	+	+
V III	a	+	+	+	
	b	+	+	+	+
N I	a	—	+	+	
	b	+	+	+	
N II	a				
	b	—	+	+	+
N III	a	—	—	+	+
	b	+	+	+	+
W I	a	—	—	+	+
	b	—	—	+	+
W II	a	—	—	+	+
	b	—	—	+	+
W III	a	—	—	+	+
	b	—	+	+	+

The foregoing Table V shows the results that were obtained. All filtrates from Berkefeld filter V yielded growths of these small bacilli, they frequently passed through filter N, while filter W arrested them under one and under two atmospheres pressure, except in portion *b* from filter III under two atmospheres pressure. Throughout the experiment contaminations were more frequent in portion *b* than in portion *a*.

CONCLUSIONS.

Although the foregoing tabulated records of experiments are very limited in extent, I feel justified in saying that with proper care immune serums can be passed through germ-proof filters without suffering any

appreciable loss of immune bodies. During the last three years large quantities of immune serums have been filtered with great success. The Berkefeld filter marked W usually furnishes a germ-free filtrate under a pressure of two atmospheres or less. If a much higher pressure is used germs appear to be forced through occasionally.

In order to avoid rapid clogging of the filter the serum should be centrifugated before filtration is attempted, and the filters must be cleansed thoroughly immediately after being used.

THE REACTION OF CULTURE MEDIA IN RELATION TO THE MORPHOLOGY OF THE CHOLERA ORGANISM.[1]

By Y. K. Ohno.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

During the previous year, on making a microscopical examination of a direct smear of the fæces from a case of cholera I was able to observe organisms which appeared to be cholera vibrios and was able to cultivate the cholera vibrio in plating a loop of the stool in 1 per cent alkaline agar. However, when a loop of the stool was first added to cholera peptone solution according to the enriching method of Schottelius-Koch,[2] I failed to isolate the cholera organism. Investigation of the peptone solution revealed the fact that its reaction upon titration was 1.75 per cent acid to phenolphthalein. The cholera vibrio, isolated from the same stool by plate culture, failed to grow in this peptone solution.

This experience led me to study the behavior of this organism in culture media of different degrees of acidity and alkalinity. I began these experiments with a few cultures of the cholera vibrio which I had at that time, and found that the vitality of the different strains varied and that the same strain changed its morphology in solutions of peptone of different reaction. The degree of acidity or alkalinity of the peptone in which the morphology of the vibrio is most likely to appear typical may be different for different strains of the cholera organism. In general, in acid media, the vibrio tends to lose its curve and to appear as a rod, while in strongly alkaline media it becomes short and appears oval or even spherical.

Having carried on experiments of this nature with the strains of the cholera vibrio on hand in the laboratory, I decided to use media of different reaction in the bacteriological examination of cholera stools and of fæces from suspected cholera cases sent to the laboratory for diagnosis during the recent epidemic. In this way I hoped to identify the cholera

[1] Read at the Sixth Annual Meeting of the Philippine Islands Medical Association, February 12, 1909, Manila, P. I.

[2] *Deutsche med. Wochnsch.* (1885), 14, 213.

vibrio even if it should appear in rod or spherical form in the 0.3 per cent alkaline peptone solution commonly used as an enriching media.[3] I first determined for a number of strains of the cholera organism, the reaction of the media in which the morphology of the vibrio was most typical, and from these experiments found that for the cultivation of cholera vibrios of typical morphology from suspected stools or other materials, at least three solutions of peptone of the following reactions should be used:

1. 0.3 per cent acid
2. 0.5 per cent alkaline
3. 1.3 per cent alkaline

} With phenolphthalein as an indicator.

From Table 1 it may be seen that some cholera strains appear as rods in 1 per cent acid peptone solution, and appear oval or spherical in form in 1 per cent alkaline peptone solution. I have also isolated a strain "Hoffman" (see Table 4) which even in a 0.5 per cent alkaline peptone solution has the bacillary form, and changes to its typical curved form only in a strong alkaline peptone of a reaction of 1.5 per cent. Strains of this nature were occasionally isolated in the bacteriological examination of cholera stools during the recent epidemic.

TABLE 1.—*The change in morphology of cholera vibrios in peptone solutions of different reactions (cultures incubated for twenty-four hours at 37° C.).*

— = clear. + = slight turbidity. + + + = marked turbidity.
± = a trace of turbidity. + + = moderate turbidity. + + + + = maximum turbidity.

No.	Reaction of peptone solution.	Strain "George."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	—	Not visible in stained preparations.
2	Acid, 1.0 per cent	±	Several small slender rods.
3	Acid, 0.5 per cent	+	The rods are slightly curved and larger than in No. 2.
4	Neutral	+ +	Moderately curved organisms, somewhat thick, both ends sharp.
5	Alkaline, 0.5 per cent	+ + +	Typical vibrios with some oval forms.
6	Alkaline, 1.0 per cent	+ +	The vibrios are thicker and less curved than in No. 5. Some oval forms are present.
7	Alkaline, 1.5 per cent	+	Cocco-bacilli; here and there arranged like diplococci.
8	Alkaline, 2.0 per cent	±	Cocco-bacilli which are smaller than those in No. 7.
9	Alkaline, 2.5 per cent	—	Not visible in stained preparations.

[3] Kolle u. Wassermann: Handbuch der pathogenen Mikroorganismen (1903) 3, 38.

TABLE 1.—*The change in morphology of cholera vibrios*—Continued.

— = clear. + = slight turbidity. + + + = marked turbidity.
± = a trace of turbidity. ┤ = moderate turbidity. + + + + = maximum turbidity.

No.	Reaction of peptone solution.	Strain "Valentine."	
		Turbidity.	Morphology.
1	Acid, 1,5 per cent	± ?	Not visible in stained preparations.
2	Acid, 1.0 per cent	± ?	Not visible in stained preparations.
3	Acid, 0.5 per cent	+	Small, straight, slender rods.
4	Neutral	+ + +	For the most part curved, some straight.
5	Alkaline, 0.5 per cent	+ + +	Typical vibrios, somewhat short and thick.
6	Alkaline, 1.0 per cent	+ + + +	Thick and short organisms, approaching the oval form.
7	Alkaline, 1.5 per cent	+	For the most part oval forms, a few curved.
8	Alkaline, 2.0 per cent	± ?	Very short bacilli and some spherical forms.
9	Alkaline, 2.5 per cent	± ?	A few coccus forms.

No.	Reaction of peptone solution.	Strain "Mendoza."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	± ?	Not visible in stained preparations.
2	Acid, 1.0 per cent	± ?	Small oval bacilli.
3	Acid, 0.5 per cent	±	Organisms longer than in No. 2.
4	Neutral	+ + +	Curved forms appear.
5	Alkaline, 0.5 per cent	+ + + +	For the most part curved; some rods.
6	Alkaline, 1.0 per cent	+ + +	Organisms all typical and thick.
7	Alkaline, 1.5 per cent	+	Very thick and short, some have the oval form.
8	Alkaline, 2.0 per cent	+	All organisms have the oval form.
9	Alkaline, 2.5 per cent	±	Spherical forms.

Five years ago Kolle and Gotschlich published a report on the bacteriological diagnosis of Koch's cholera vibrio. They collected 65 strains of the cholera organism and were able to prove that all of these strains could be identified by the reactions of agglutination and bacteriolysis with a cholera immune serum. Although these strains did not differ in their biological characteristics, yet they did show morphological differences. Table 2 indicates the morphology of the strains studied by Kolle and Gotschlich.[4]

[4] *Ztschr. f. Hyg.* (1903), 44, 1.

TABLE 2.—*Differentiation of the cholera vibrio according to its morphology into four groups.*

I. GROUP "RODS."

Series.	Morphology of the cholera strains studied by Kolle and Gotschlich.	Number of strains collected.	Percentage.
1	Moderately long curved rods	7	
2	Short well-curved rods	7	
3	Very long slender rods	1	41.535
4	Long, slender and curved rods	6	
5	Moderately long and moderately slender rods	6	

II. GROUP "VIBRIO."

6	Rather long and thin, very slightly curved	1	
7	Moderately long, curved	9	
8	Fairly well curved	1	
9	Fairly well curved	2	
10	Short, only slightly curved	3	40.000
11	Very short, curved	2	
12	Short, curved	4	
13	Well curved, very short	1	
14	Short, moderately slender	2	

III. GROUP "COMMA FORM."

15	Thick and short	3	
16	Moderately long comma	2	15.353
17	Short	4	
18	Short, slender	1	

IV. GROUP "COCCO BACILLUS."

19	Short, almost a coccus	1	4.616
20	Short and thick	2	
	Total	65	

	Per cent.	Per cent.
Cocci form, Group IV	= 4.616	16.923
Bacillus form, series 3+5+6	=12.307	
Curved form, series 1+2+4	=30.768	
Total	57.691	

With regard to morphology, the cholera organism may be said to assume four forms:

1. The bacillary form, which varies in length and thickness.

2. The typical vibrio form, which shows variation in the degree of curving, in length, and in breadth.

3. The "comma form," with variation only in regard to length and thickness.

4. The "coccus form," which varies in its diameter assuming sometimes an oval form and then again a spherical one.

A most important factor in the campaign against an epidemic of cholera is the discovery of every source and locality of infection. The finding and disinfection of these sources is accomplished by the detection of the cholera vibrio in stools, waters, sewage, and other places, and its morphology may be a very important factor in its detection. In stained preparations from cultures in peptone, or even in those made directly from the stools, the form of the vibrio is often the starting point in the detection of the cholera organism. If we examine Table 2, we perceive that in 4.616 per cent of the different strains of the cholera vibrio this organism assumed the coccus form, while in 12.307 per cent it appeared as a rod. Therefore, if we should neglect the further examination by means of plate cultures and the performance of the agglutinative and bacteriolytic reactions, we would fail in the detection of the cholera vibrio in 16.923 per cent of the cases. Moreover, if we pursue the complete bacteriological investigation only in those cultures in which the typical vibrio form is present, we would fail in the detection of the cholera organism in 57.691 per cent of the cholera cases. Therefore, in the examination of suspected material for the cholera organism, much assistance can frequently be given if the three solutions of peptone of different reactions are employed, since in one of these it is very likely that the organism will assume its typical vibrio form.

It seems to me that most authors do not lay sufficient stress upon the reaction of the peptone solution used in isolating the cholera vibrio. It is usually merely stated that the peptone solution should be slightly alkaline. In Prussia, 0.3 per cent of crystallized soda after neutralization to litmus, is employed for the media, and most German authors agree that this is the optimum reaction for the media; that is, 0.3 per cent alkaline to litmus. Lehmann[5] thinks it is preferable to use 2 per cent normal sodium hydroxide, or 1 per cent crystallized or 0.3 per cent water free soda after neutralization with phenolphthalein. However, with peptone solution of but one degree of alkalinity as stated above, it is not uncommon to fail to discover cholera vibrios from the microscopical examination owing to the fact that they do not appear in typical form.

[5] Lehmann & Neumann: Bacteriologische Diagnostik. Munich, 4th ed. (1907) 487.

TABLE 3.—*Showing the development of cholera vibrios from suspected cholera stools in peptone solutions of different reaction.*

	Reactions.					Reactions.				
	Number of strain.	Acid 0.3 per cent.	Alkaline 0.5 per cent.	Alkaline 0.5 per cent.	Cholera?	Number of strain.	Acid 0.3 per cent.	Alkaline 0.5 per cent.	Alkaline 1.5 per cent.	Cholera?
Development	36	+	+	+	+	42	++	++	+++	+
Form		—	—	)			)	)	)	
Indol		—	—	—			—	—	—	
Development	37	++	+±	+±	+	43	++	++	±	
Form		)	)	)			—	?	)	
Indol		±	—	—			—	—	+	
Development	38	+±	—	—	—	44	++	++	++	+
Form		—	—	?			)	)	)	
Indol		+	—	—			—	+	+	
Development	39	+			+	45	)	)	)	+
Form		)	—	—			)	)	)	
Indol		—	—	—			—	+	—	
Development	40	+	+	+±	—	46	++	++	±	+
Form		—	—	)			)	)	?	
Indol		—	±	—			—	—	+	
Development	41	++	++	++	—	47	+++	++	+++	+
Form		—	—	)			?	)	?	
Indol		—	±	—			—	+	+	

)Indicates the presence of comma-shaped vibrios.

It is very easy to make a bacteriological diagnosis from typical cholera stools, and, after the organisms have been obtained in pure culture, it is not difficult to differentiate and identify them by means of agglutinative and bacteriolytic reactions; however, it is nevertheless very difficult to isolate the cholera vibrio when it is present in very small numbers in the suspected material, the reaction of which is unknown and in which the organism sometimes appears with a different morphology.

If, in the beginning of a bacteriological examination, microscopical preparations are made from the fæces directly or from the peptone used for enriching, we may fail sometimes entirely to recognize the presence of the cholera vibrio in such preparations because of the divergent morphology which it may assume, and therefore neglect further to pursue the bacteriological examination. Therefore during a cholera epidemic where it is necessary to examine bacteriologically a very large number of specimens of fæces for diagnosis, my proposal to use culture media of three different degrees of alkalinity or acidity so that the different strains of the cholera vibrio will appear in typical vibrio or comma form in at least one of them, notwithstanding the

original form of the strain, is, I believe, a distinct aid and advance in the bacteriological diagnosis of cholera and therefore will be of assistance in the suppression of a cholera epidemic.

From my investigations it would appear that the different strains of the cholera vibrio may be arranged, with reference to their resistance to acid and alkali, into four groups:

1. Cholera vibrios resistant to acid solutions but not resistant to alkaline ones.

2. Cholera vibrios resistant to alkaline solutions but not resistant to acid ones.

3. Cholera vibrios resistant to both alkaline and acid solutions.

4. Cholera vibrios not resistant to either alkaline or acid solutions.

By *resistance* is meant the power of the organism to grow and to multiply in the culture medium in question in a typical form.

TABLE 4.—*Types of cholera vibrios developing typical morphology, (1) in highly alkaline media, (2) in acid media, (3) in both alkaline and acid media, (4) in neutral media.*

Series of tubes, peptone solution.	Reaction of media.	(1) "Hoffman."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	—	Not visible.
2	Acid, 1.0 per cent	—	Not visible.
3	Acid, 0.5 per cent	—	Not visible.
4	Neutral	—	Not visible.
5	Alkaline, 0.5 per cent	++++	Bacillary form, some slightly curved.
6	Alkaline, 1.0 per cent	+	Thick and short, with slight curve.
7	Alkaline, 1.5 per cent	+	Typical comma forms.
8	Alkaline, 2.0 per cent	±?	Spherical forms.
9	Alkaline, 2.5 per cent	—?	Few spherical forms.

Series of tubes, peptone solution.	Reaction of media.	(2) "Felix II."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	+	Half in straight form, half in curved form, size small.
2	Acid, 1.0 per cent	+	Half in straight form, half in curved form, size small.
3	Acid, 0.5 per cent	++	Mostly typical comma forms.
4	Neutral	+++	Organisms thick and short, mostly of oval form.
5	Alkaline, 0.5 per cent	+++	Thicker and shorter, a few curved forms, the majority like cocci.
6	Alkaline, 1.0 per cent	+	Oval or coccus forms.
7	Alkaline, 1.5 per cent	±	Spherical forms.
8	Alkaline, 2.0 per cent	±?	Spherical forms.
9	Alkaline, 2.5 per cent	—?	Very few spherical forms.

TABLE 4.—*Types of cholera vibrios developing typical morphology*—Continued.

Series of tubes, peptone solution.	Reaction of media.	(3) "Helmon I."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	+	Very few straight forms.
2	Acid, 1.0 per cent	+	Slightly curved forms.
3	Acid, 0.5 per cent	+ +	Comma forms, numerous spirilla.
4	Neutral	+ + +	Typical comma forms, no spirilla.
5	Alkaline, 0.5 per cent	+ + +	Typical, spirilla.
6	Alkaline, 1.0 per cent	+ +	Typical, comma forms.
7	Alkaline, 1.5 per cent	±	Typical, comma forms.
8	Alkaline, 2.0 per cent	±	Short, curved and some oval forms.
9	Alkaline, 2.5 per cent	+	Spherical forms.

Series of tubes, peptone solution.	Reaction of media.	(4) "Juan I."	
		Turbidity.	Morphology.
1	Acid, 1.5 per cent	+	Very few thin, short rods.
2	Acid, 1.0 per cent	+	A few rods and a few oval forms.
3	Acid, 0.5 per cent	+ ±	Curved rods.
4	Neutral	+ +	Rods slightly curved.
5	Alkaline, 0.5 per cent	+ +	Curved, rods and oval forms.
6	Alkaline, 1.0 per cent	+ +	Oval and spherical forms.
7	Alkaline, 1.5 per cent	±	Short, small forms.
8	Alkaline, 2.0 per cent	±	Not visible.
9	Alkaline, 2.5 per cent	±	Not visible.

It is a striking fact that the reaction of the typical cholera stool generally agrees with the reaction of the peptone solution in which the typical form of that strain of cholera vibrio occurs. I have examined the reaction of 26 typical cholera stools in all of which cholera vibrios were found, and I was able to ascertain that most of them (that is, 73 per cent) showed an alkaline reaction (the maximum corresponding to 0.88 per cent normal caustic soda), while about 20 per cent were acid (the highest degree of acidity equaling 1.24 per cent of normal hydrochloric acid), and the rest (about 7 per cent) being neutral. (See Table 5.) From one sample of 1.24 per cent acidity, the typical vibrio form was not seen in 0.5 per cent alkaline peptone, but the smear from the stool showed typical vibrios, and slightly thick and short vibrios developed on 0.3 per cent acid peptone. The alkalinity of a stool which contains cholera vibrios in almost pure culture usually increases by standing a few days, and from these stools it is very difficult to cultivate cholera vibrios in typical form in acid peptone solution.

TABLE 5.

STOOLS OF ALKALINE REACTION.

No.	Name of patient.	Age.	Duration of illness before admission.	Symptoms.	Date of examination.	Reaction of stools (with phenolphthalein).	Date of admission to hospital.	Date of discharge from hospital.
						Per ct. react.		
1	Mariano Compatete	30	Unknown.	Serious	Aug. 30	0.01	Aug. 30	[a] Aug. 30
2	Mariano de la Cruz	29	3 hours	Serious	Sept. 14	0.12	[d]	Sept. 14
3	Juan de la Cruz	75	2 hours	Serious	Sept. 1	0.04	Sept. 1	[a] Sept. 1
4	Lesaria Hilacio	29	14 hours	Serious	Sept. 4	0.04	Sept. 4	[a] Sept. 4
5	Antonio Baglud	15	(?)	Serious	Sept. 4	0.12	Sept. 4	[a] Sept. 4
6	K. Abe	24	8 hours	Serious	Sept. 4	[b]	Sept. 4	[a] Sept. 4
7	Masuda	27	5 hours	Moderate	Sept. 4	0.88	Sept. 4	Sept. 18
8	Alfreda Antonio	2	2 days	Moderate	Sept. 5	0.08	Sept. 5	[a] Sept. 7
9	Feliciano Cuson	60	(?)	Moderate	Aug. 25	0.32	Aug. 25	Sept. 13
10	Marcela Euson	3	4 hours	Serious	Sept. 15	0.08	Sept. 15	[a] Sept. 15
11	Miguel Seño	23	2 hours	Serious	Sept. 8	0.20	Sept. 8	Sept. 20
12	G. Walter Garrens	29	16 hours	Serious	Sept. 9	0.24	Sept. 1	[a] Sept. 1
13	Gregorio Alcarez	23	16 hours	Moderate	Sept. 10	0.32	Sept. 10	Sept. 20
14	Masuda	27	[c]	[c]	Sept. 11	0.32	Sept. 4	Sept. 18
15	Juan Lumaban	40	6 hours	Serious	Sept. 13	0.16	Sept. 13	[a] Sept. 14
16	Bruna Zamora	40	19 hours	Serious	Sept. 15	0.12	Sept. 15	[a] Sept. 16
17	Elocia	30	4 days	Serious	Sept. 15	0.04	Sept. 15	[a] Sept. 15
18	Engracia Estada	8	4 days	Moderate	Sept. 13	0.12	Sept. 13	[a] Sept. 17
19	Bartolome de Mendoza	45	10 hours	Serious	Sept. 13	0.07	Sept. 13	[a] Sept. 17

STOOLS OF NEUTRAL REACTION.

20	Raymundo Legaspi	23	12 hours	Serious	Sept. 8	[c]	Sept. 8	[a] Sept. 9
21	Ambrocio Salvador	5	18 hours	Moderate	Sept. 13	[c]	Sept. 13	Sept. 20

STOOLS OF ACID REACTION.

22	Pedro Dominguez	53	16 hours	Serious	Sept. 5	0.02	Sept. 5	Sept. 10
23	Felix Siamingo	18	4 hours	Serious	Sept. 13	0.01	Sept. 13	Sept. 21
24	Ciriaco Eunion	29	3 days	Serious	Sept. 15	1.24	Sept. 15	[a] Sept. 16
25	Leoncio Rogue	44	20 hours	Serious	Sept. 16	0.12	Sept. 16	[a] Sept. 16
26	Alfonso Leonardo	50	17 hours	Serious	Sept. 20	0.40	Sept. 19	[a] Sept. 21

[a] Died.
[b] Slightly alkaline.
[c] Neutral.
[d] Transferred to Mary Johnston Memorial Hospital.
[e] Second specimen.

Acidity average, 0.39 per cent.

Percentage of stools with acid reaction.....=19.22
Percentage of stools with alkaline reaction.....=73.09
Percentage of stools with neutral reaction.....= 7.69

From the experiments given in the tables above it may be seen that different strains of the cholera vibrio react differently toward acid and alkaline solutions, and that the medium in which the morphology appears most typical is different for the different strains. Therefore, it follows that peptone solutions of different reaction should be used in isolating the cholera organism in cultures, and, as I have stated, I believe that at least three different peptone solutions are necessary to obtain the best results.

The cholera vibrio shows a great adaptability to culture media of different reaction. For example, if we inoculate a strain of the cholera vibrio into 2.5 per cent alkaline peptone solution in which the organism at first develops but slightly and appears in a spherical form, in the course of a number of passages through peptone of the same reaction the rapidity of growth in this media increases and it finally regains its original size and thickness and its typical form. (See Table 6.)

TABLE 6.—*Adaption of cholera vibrio to alkaline media.*

Strain.	First generation.	Third generation.	Fifth generation.	Eighth generation.
"Margarita I".	Slight development of spherical forms.	Slight development, some curved, some oval forms.	Development moderate, most forms curved, some oval.	Well developed, typical forms.
"Juan"	Very slight development of spherical forms.	Slight development, some curved, some oval forms.	Development moderate most forms still oval.	Well developed, typical forms.
"Engracia I".	Slight development of spherical, oval and thick curved forms.	Development moderate, most forms curved and of still smaller size.	Development marked, most forms curved, thick, and large.	Well developed, typical forms.
"Leon I"	Slight development of coccus forms.	Slight development, all oval forms.	Development moderate, some oval, some curved forms.	Well developed, all forms curved, thick, and short.

This adaptability can also be demonstrated in a single inoculation of the culture media, when the quantity of peptone present is sufficient to furnish nutritive material to the strain for a long period of time. The adaption takes place slowly, so that if we inoculate a strain which is highly adapted to an alkaline medium on acid culture media, the morphology of the vibrio changes at first to that of a rod or to an oval or spherical form. When this strain is adapted on the acid medium, on re-inoculating it on the original alkaline culture media it appears in oval or spherical form even if its morphology was typical formerly on this.

TABLE 7.—*Changes in morphology in a typical cholera vibrio from 0.5 per cent alkaline peptone first transferred to 2.5 per cent alkaline peptone for various periods of time and then to 0.3 per cent acid peptone, and to 1.0 per cent acid agar.*

Generation.	Morphology when transferred to 2.5 per cent alkaline peptone.		Morphology when transferred to 0.3 per cent acid peptone.	Morphology when transferred to 1 per cent acid agar.
	Transfered.	Left standing.		
First	Spherical forms first day.	After 10 days, typical forms.	Spherical or oval form, very few curved.	Mostly cocci, a few oval forms.
Second	Oval forms, first day.	After 8 days, typical.	Spheres or oval and thick forms.	Spherical or oval forms, a few curved rod forms.
Third	Oval rods, first day.	After 6 days, typical forms.	Spheres or oval and thick forms.	Few spherical forms, oval and rods forms.
Fourth	Curved rods, fourteenth day from the first generation.	After 4 days, typical forms.	Few spherical forms, mostly curved short forms.	Oval and rod forms some curved forms.
Fifth	Typical forms, fifteenth day from the first generation.	After 2 days, typical forms.	Mostly curved forms, a few oval or rod forms.	Rods most of them curved.

All show moderate development.

Luxuriant growth.

From Table 7 it may be seen that all the strains of the cholera vibrio show variations in morphology in the culture media of different reaction, and that each has no constant form in any one culture medium until after its adaption to that medium has become complete. After the cholera vibrio has become adapted to media of high alkalinity or high acidity and grows in typical form in such media, if it is then transplanted to media of a neutral reaction, it assumes an atypical or spherical form. This variability in the morphology of the cholera vibrio seems to justify the employment of three peptone solutions of different reaction for the routine technique in the isolation of this organism. I do not claim that the reaction of the culture medium is the only factor that gives rise to pleomorphism in the cholera vibrio; there are probably other factors which also do this and this question should be investigated further.

No relationship between the production of indol on the one hand and the reaction of the culture medium and the morphology of the cholera organism on the other could be established. (See Tables 8 and 9.) For this reason the indol reaction is not of great assistance in the diagnosis of the cholera vibrio.

TABLE 8.—*Relation between the reaction of the peptone solution and the production of indol.*

Series of tubes.	Hoffman.		Felix II.		Helmon I.		Juan I.		Reaction of tubes.
	Development.	Indol.	Development.	Indol.	Development.	Indol.	Development.	Indol.	
1	—	—	+	—	+	—	+	—	Acid, 1.5 per cent.
2	—	—	+	+	+	+	+	+	Acid, 1.0 per cent.
3	—	—	++	—)	++	—)	+±	—	Acid, 0.5 per cent.
4	—	—	+++	++	+++	—)	++	+)	Neutral.
5	++++	—	+++	++	+++	++)	++	+)·	Alkaline, 0.5 per cent.
6	+	—)	+	—	++	—)	++	—	Alkaline, 1.0 per cent.
7	+	+)	±	+	±	—)	±	—	Alkaline, 1.5 per cent.
8	±?	—	±?	—	+	—	±	—	Alkaline, 2.0 per cent.
9	—?	—	—?	—	+	—	±	—	Alkaline, 2.5 per cent.

)Indicates typical morphology of the cholera vibrio.

TABLE 9.—*Examination of stools from individuals who had been in contact with cholera patients (no cholera vibrios present); showing the development of other vibrios, than the cholera vibrio, when cultivated in the 3 peptone solutions of different reaction and their relation to the production of indol.*

	Number of strain.	Reaction. Acid, 0.3 per cent.	Alkaline, 0.5 per cent.	Alkaline, 1.5 per cent.	Cholera?	Number of strain.	Reaction. Acid, 0.3 per cent.	Alkaline, 0.5 per cent.	Alkaline, 1.5 per cent.	Cholera?
Development	60	++	++	++	—	66	++	++	±	—
Form of vibrio		—	—	)			—	)	—	
Indol		—	—	±			±	—	—	
Development	61	++	++	+++	—	67	++	++	+++	—
Form of vibrio		—	)	—			)	)	)	
Indol		—								
Development	62	++	++	++	—	68	++	++	++	—
Form of vibrio		—	—	—			)	)	)	
Indol		—	—	±			+	—	—	
Development	63	+++	++	+++	—	69	+++	+	±	—
Form of vibrio		—	—	—			)	)	)	
Indol		—	—	±			+	—	—	
Development	64	++	++	++	—	70	+++	++	±	—
Form of vibrio		)	)	)			)	)	—	
Indol		—	—	±			—	—	+	
Development	65	++	++	+	—	71	+++	++	±	—
Form of vibrio		—	)	—			—	—	—	
Indol		±	—	—			+++	—		

As to the relation between the cholera vibrio in culture media of different reaction and its agglutinability, it would appear from the results of my experiments that the more the acidity or alkalinity of the media is increased the more the agglutinability of the organism is decreased. Further observations on this question are now being pursued.

IMMUNIZING CATTLE AGAINST ANTICATTLE-PLAGUE SERUM.

By E. H. Ruediger.

(From the Serum Section of the Biological Laboratory, Bureau of Science, Manila, P. I.)

In connection with the formation of antibodies after injections of anticattle-plague serum, it has been stated that animals that have been repeatedly inoculated with anticattle-plague serum eventually become more susceptible to infection with the disease. While the views of the author did not coincide with such an idea, nevertheless, as the question was one of considerable practical importance, it was thought advisable to investigate this question by experiment.

It is an established fact that certain immune substances present in the serum of one species of animal, when injected into an animal of another species lead to the production of antiimmune substances.

Metschnikoff,[1] in 1900, injected spermotoxic serum of guinea pigs into rabbits, and, after so treating the rabbits for a short period of time, found that their serum had acquired the property of neutralizing or peventing the toxic action of the spermotoxic guinea pig serum upon spermatozoa. Weichart[2] also obtained antispermotoxic serum by treating animals with spermotoxic serum.

Metschnikoff,[3] Ehrlich,[4] Mueller[5] and others produced antihæmotoxin (hæmolysin) by treating animals with haemotoxic serum.

The subject of antiimmune bodies soon became an important one from a practical as well as from a scientific standpoint. Diphtheria antitoxin, tetanus antitoxin, antiplague serum and other immune serums, are frequently given to persons who have been exposed to the respective diseases, and if antiimmune substances were produced such prophylactic treatment would become detrimental instead of beneficial.

Kraus and Eisenberg[6] treated rabbits, dogs and goats with diphtheria antitoxin, typhoid agglutinating serum, and with lactoserum. The serum

[1] *Ann. Inst. Pasteur.* (1900), **14**, 1.
[2] *Ann. Inst. Pasteur.* (1901), **15**, 832.
[3] *Bull. de l'Acad. de Med.* (1909), **43**, 598.
[4] *Berlin klin. Woch.* (1901), **38**, 569.
[5] *Centralbl. f. Bakt.* (1901), I, **29**, 175.
[6] *Ibid.* (1902), I, **31**, 208.

of animals which had been treated with diphtheria antitoxin or with typhoid agglutinating serum did not possess any substances which neutralized or prevented the action of the respective antitoxin or agglutinin. On the other hand, the serum of animals which had been treated with lactoserum, when mixed with lactoserum prevented the action of the latter upon milk. The authors conclude:

I. Immune substances, as diphtheria antitoxin and typhoid agglutinin, can not lead to the production of antibodies when injected into an animal.

II. Treating an animal with lactoserum produces antilactoserum.

It must be borne in mind that practically all of our ideas concerning the production of antibodies are based upon experimental work relating to bacterial diseases and that the nature of the causative agent of cattle plague is as yet entirely unknown. It is therefore possible that the protective substances of anticattle plague serum are radically different from the antibodies with which we are acquainted and have a different mode of action. According to current notions, it is theoretically impossible to obtain antibodies by injecting an antiserum obtained from one animal into another animal of the same species. Nevertheless, cattle were used in these experiments both for the production of the anticattle-plague serum and in the attempt to obtain a serum antagonistic to the anticattle-plague serum. This plan was pursued primarily as has been intimated because of the imminently practical question as to whether or not overimmunization could lead to the production of susceptibility to the disease. However, it was also desirable to observe whether the laws of immunity involved were the same for cattle plague as they were for bacterial infections.

The following experiments were performed to show whether or not substances which render inert anticattle-plague serum are produced when the latter is injected at intervals into cattle.

EXPERIMENTAL.

Nine bullocks, non-immune to cattle plague, numbered 16, 17, 18, 19, 20, 22, 23, 24, and 25 were used.

Bullocks Nos. 16, 17, 18, 19 and 20 remained untreated; Nos. 22, 23, 24 and 25 received three injections of 100 cubic centimeters each of anticattle-plague serum at intervals of ten days. On the 28th day of June, these bullocks were subjected to the simultaneous method of immunization, bullock No. 16 acting as control.

Bullock No. 16 received 0.5 cubic centimeter of virulent blood under the skin and died of cattle plague within eleven days after inoculation. (Chart No. 16.)

Bullock No. 17 received 0.5 cubic centimeter of virulent blood, and 50 cubic centimeters of anticattle-plague serum per 100 kilos weight and died of cattle plague within eleven days after inoculation. (Chart No. 17.)

Bullock No. 18 was inoculated with 0.5 cubic centimeter of virulent blood and 75 cubic centimeters of anticattle-plague serum on the 28th day of June and was found dead on the morning of July 10th. (Chart No. 18.)

Bullock No. 19 inoculated with 0.5 cubic centimeter of virulent blood and 100 cubic centimeters of anticattle-plague serum died twelve days after inoculation. (Chart No. 19.)

Bullock No. 20 died within fourteen days after having received 0.5 cubic centimeter of virulent blood and 125 cubic centimeters of anticattle-plague serum under the skin. (Chart No. 20.)

Bullock No. 22 received 0.5 cubic centimeter of virulent blood and 50 cubic centimeters of anticattle-plague serum. He developed typical cattle plague from which he recovered. (Chart No. 22.)

Bullock No. 23, after inoculation with 0.5 cubic centimeter of virulent blood and 75 cubic centimeters of anticattle-plague serum, had a mild attack of cattle plague from which a good recovery was made. (Chart No. 23.)

Bullock No. 24 received an inoculation of 0.5 cubic centimeter of virulent blood and 100 cubic centimeters of anticattle-plague serum. A very mild attack of cattle plague followed from which an uneventful recovery resulted. (Chart No. 24.)

Bullock No. 25, having received 0.5 cubic centimeter of anticattle-plague serum, showed a slight rise of temperature and made a rapid recovery. (Chart No. 25.)

The results are summarized in the following table.

Number of bullocks.	Virulent blood.	Serum.	Result.	Remarks.
16	0.5	None.	Died	Control.
17	0.5	50	Died	Not treated previously.
18	0.5	75	Died	Not treated previously.
19	0.5	100	Died	Not treated previously.
20	0.5	125	Died	Not treated previously.
22	0.5	50	Lived	Treated previously.
23	0.5	75	Lived	Treated previously.
24	0.5	100	Lived	Treated previously.
25	0.5	125	Lived	Treated previously.

CONCLUSION.

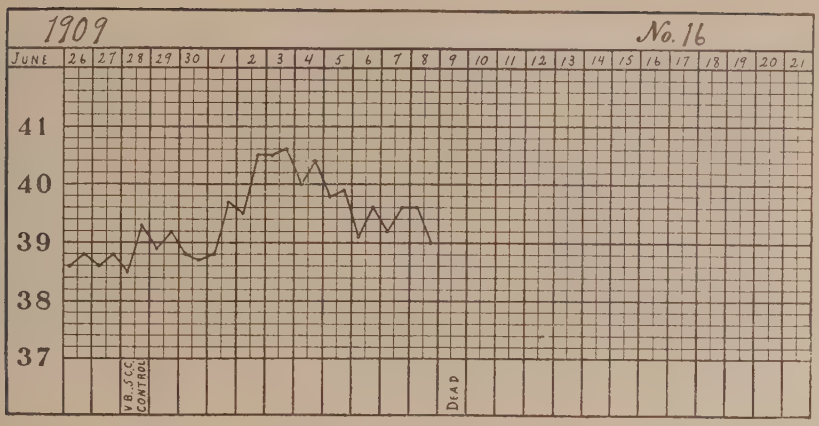
Apparently anticattle-plague serum, when repeatedly injected under the skin of healthy, non-immune bullocks, does not lead to the production of antiimmune bodies.

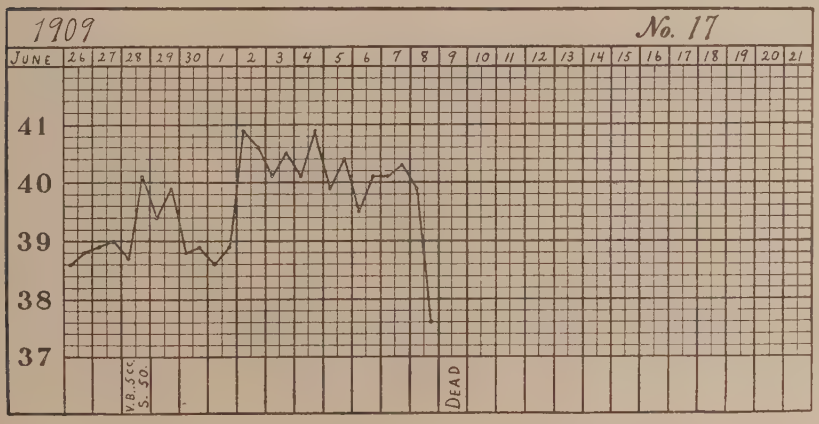
The more serum injected into an animal the milder is the attack of cattle plague which follows inoculation with virulent blood.

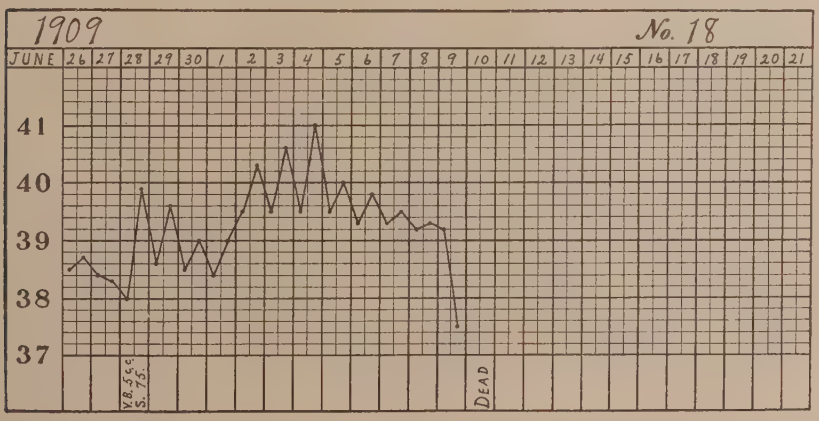
In this respect the immunity reactions in cattle plague are similar to those observed in many infections of known bacterial origin.

ILLUSTRATIONS.

Temperature charts Nos. 16–25. 357


1909
No. 16
JUNE 26 27 28 29 30 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
41
40
39
38
37
V.B. Scc. CONTROL
DEAD


1909
No. 17
JUNE 26 27 28 29 30 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
41
40
39
38
37
V.B. Scc. S. 50
DEAD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No. 18
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41
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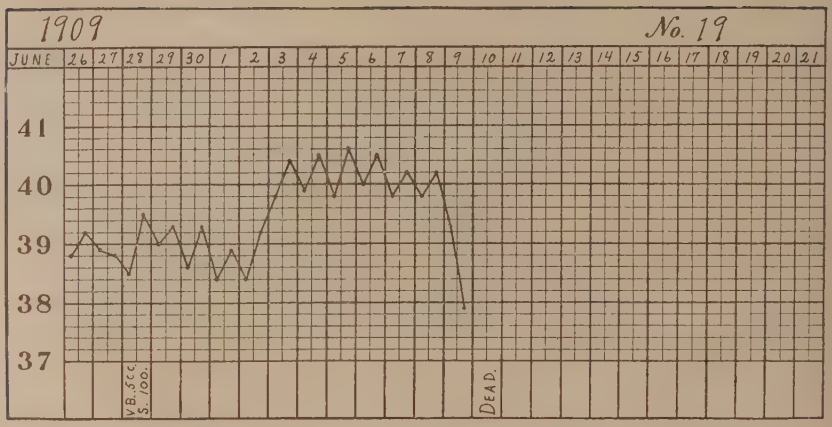
38
37
V.B. Scc. S. 75
DEAD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No. 19
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41
40
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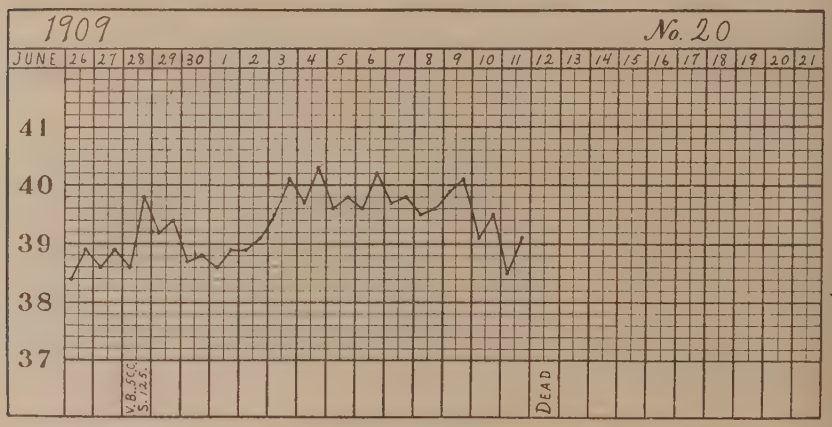
38
37
V.B. SCC. S. 100.
DEAD.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No. 20
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41
40
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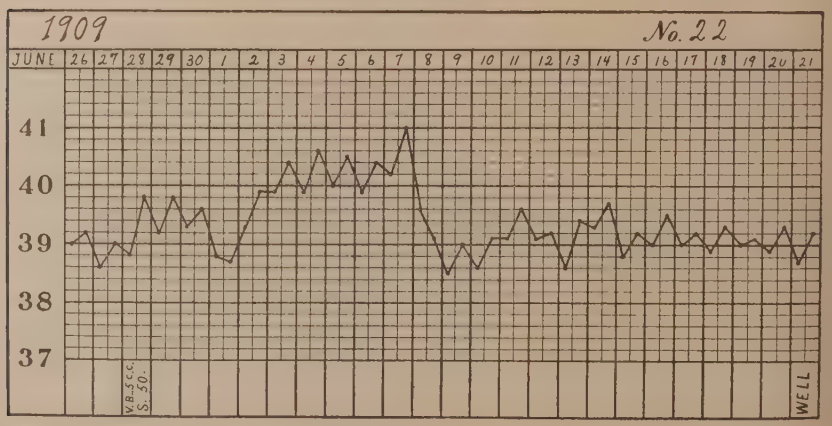
38
37
V.B. SCC. S. 125.
DEAD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41
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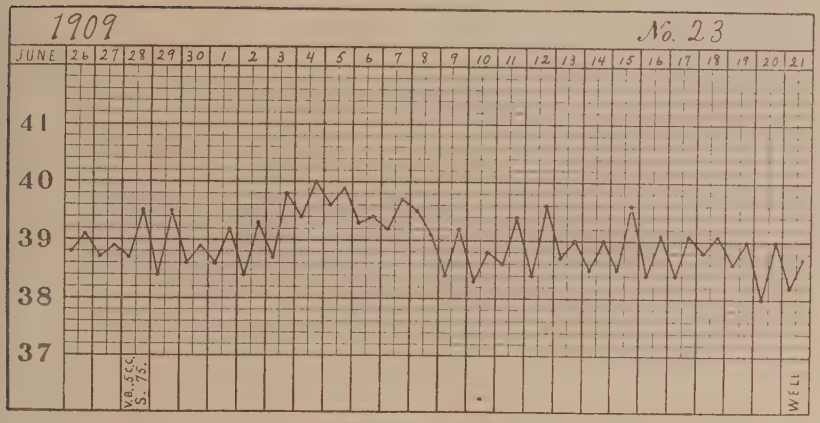
37
V.B.S.CC. S. 50.
WELL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37
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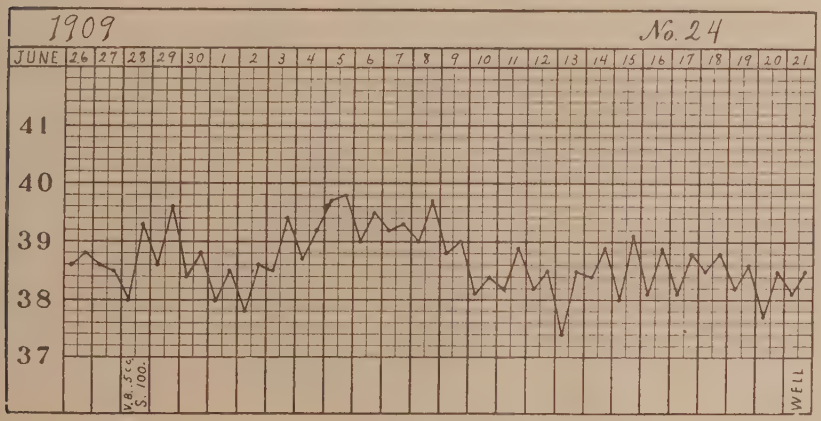
WELL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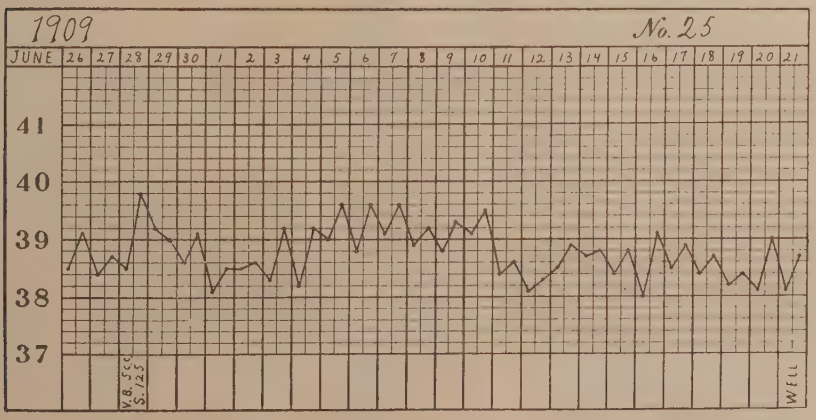
41
40
39
38
37
V.B. 5 c.c. S. 100.
WELL


1909
No. 25
JUNE 26 27 28 29 30 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
41
40
39
38
37
V.B. 5 c.c. S. 125.
WELL

SOME OBSERVATIONS UPON CHOLERA IN CHILDREN.

By ALLAN J. MCLAUGHLIN.[1]

(*From the Bureau of Health.*)

There is no reason for believing children to be less susceptible to cholera than adults, especially in view of the fact that children are particularly prone to all other intestinal disorders.

Statistics of incidence in children in Manila under 10 years of age of certain diseases during the three years 1907, 1908, 1909.

	Percentage of cases.
Meningitis [a]	96.80
Enteritis	93.14
Dysentery	63.66
Cholera	22.82

[a] Meningitis is here included with the intestinal diseases of children because we are able to show that real acute meningitis is rare and that the disease diagnosed by Filipino physicians as acute meningitis is usually an intestinal infection with marked cerebral manifestations.

During cholera epidemics in the Philippines, about 22 per cent of the reported cases of cholera occur in children, while the increase of deaths among children from other diseases is remarkable. By examining the following tables and charts, it will be seen that the notable increase in the deaths of children from meningitis, enteritis, and dysentery in Manila is coincident with or that it immediately precedes an epidemic of cholera, and that the increase is not dependent upon the season, as it occurs in January and February as well as in July, August, or September.

Owing to the investigations made by the writer in the past three months upon deaths in children from meningitis, enteritis, and dysentery, more care has been exercised in making the diagnosis upon the death certificates of children, and many cases were sent to San Lazaro Hospital as cholera which probably formerly would have been classified as enteritis, meningitis, or dysentery. Thus, the percentage of cholera cases reported in children under 10 years of age during the past outbreak was

[1] Passed assistant surgeon, United States Public Health and Marine-Hospital Service, Assistant Director of Health, Manila.

raised to 32.5 per cent, while the usual incidence in children has been 22 per cent. For this reason, the upward curve upon the charts of meningitis, enteritis, and dysentery of the last quarter does not show so sharp a rise coincident with the cholera outbreak.

There is no foundation for the theory that cholera vibrios live outside of the human body for months during the inter-epidemic periods. There is scientific evidence to show that this is improbable if not impossible. It has been demonstrated also that the duration of cholera vibrios in the human intestine is limited, both in true cases of cholera and in "vibrio carriers." In the majority of cases the duration is less than ten days.

The periods of quiescence between epidemics vary from several months to years. One hears constantly in the Philippines the statement that cholera always recurs in the same places, the inference being that the infection lies dormant for months or years and suddenly, under favorable conditions, breaks out in epidemic form. There is no scientific evidence to support such an inference. On the contrary, one outbreak of cholera can be traced practically always to another source of infection in a neighboring province. In the few apparent exceptions, our failure to trace the source of infection is probably due to our inability to find the connecting links in the chain of infection. During the past eighteen months, I have never known of an outbreak of cholera which was not traceable to some known source of infection, either by direct conclusive evidence or by reasonable logical deduction.

Where the periods between epidemics last for several months or for years, the beginning of an outbreak in the locality is due to infection introduced from outside. In quiescent periods of less than two months duration, the infection has been re-introduced or has been continuously present in persons with light or with atypical symptoms of cholera.

Three classes of unreported cases may be responsible for continuing the infection of cholera from one outbreak to another, where the interval between the outbreaks is short but of more than five days' duration:

1. Cases without symptoms. ("Vibrio carriers.")
2. Cases with slight symptoms.
3. Cases with atypical symptoms.

During epidemics, the importance of the "vibrio carrier" in spreading infection can not be overestimated, but the presence of the "vibrio carrier" can not be depended upon to explain all periods of quiescence of the disease, especially as such individuals are rare except during an epidemic of cholera.

It is well known that light cases of cholera occur with no symptoms beyond vomiting and a slight diarrhœa, and that they may be confused readily with an attack of acute gastro-enteritis. However, the atypical cases of cholera in children are of far greater importance.

The reporting of cases of communicable disease in the Philippines is compulsory under the Sanitary Code. Living cases, especially light ones, may go unreported or unrecognized and the error not be discovered. In fatal cases, the Bureau of Health has more perfect control. All interments necessitate a burial permit from the Bureau, and before granting this a death certificate from a municipal or a private physician, countersigned by a medical inspector of the Bureau of Health, is necessary. These death certificates are scrutinized very closely at the central office of the Bureau. Practitioners might interchange the diagnosis as between cholera and acute enteritis, but they would scarcely dare to attempt gross deception. The cases of cholera which have not been reported as such have been reported usually as acute or chronic gastro-enteritis, enteritis, entero-colitis, acute or chronic dysentery, and acute meningitis.

It was noted that the deaths from the above causes always increased just before or during an outbreak of cholera. I decided to investigate these fatal cases, and the results given below corroborated my suspicion that cholera cases were frequently unrecognized and unreported in Manila. Some of these cases were sent to the morgue for autopsy; in others, samples of the intestinal contents were taken in lieu of an autopsy. The following cases are examples:

Case 1.—D. G.—Age, 1 year 8 months. Male. Duration of illness, three months. Diagnosis and history by municipal physician. Diagnosis, chronic gastro-enteritis. Absence of symptoms of cholera other than diarrhœa of a fæculent character. Post-mortem findings obscured by decomposition of organs. Cholera vibrio recovered from intestinal contents.

Case 2.—T. P.—Age, 3 years. Male. Case diagnosed as chronic enteritis, of six months' duration. No vomiting, cramps, or other symptoms of cholera. Diagnosis and history by Dr. L. L. Specimen taken from intestine positive for cholera vibrio.

Case 3.—J. V.—Age, 5 years. Female. Diagnosis and history by municipal physician, Dr. H. Diagnosis, acute dysentery. Duration of illness, fifteen days. Diarrhœa, bloody stools, no vomiting or other symptoms of cholera. Post-mortem findings atypical of cholera. Examination of intestinal contents positive for cholera vibrios.

Case 4.—D. E.—Age, 6 years. Female. Diagnosis, chronic enteritis. Duration, three months. None of the symptoms of cholera were present except diarrhœa, the stools were not of a rice-water character. Diagnosis and history by Dr. B., a private physician. Post-mortem findings, acute specific enteritis, cloudy swelling of the kidneys and other lesions suggestive of cholera. Examination of intestinal contents positive for cholera.

Case 5.—F. S.—Age, 2 years. First appearance of illness, August 7. Visited by municipal physician August 14. Patient weak, thin. Diarrhœal stools, two to 3 a day. Slight fever. Above conditions continued, gradually reducing the child's strength until on August 25 a slight cough and vomiting began. Some meteorism and great emaciation. No meningeal symptoms noticeable. History and diagnosis of acute enteritis by Dr. C., municipal physician. Examination of intestinal contents positive for the cholera vibrio.

Case 6.—A. C.—Age, 3 years. Male. Diagnosis, enteritis and meningitis. Presented no symptoms other than diarrhœa until the last twenty-four hours. Duration of illness, ten days. On the last day, convulsions, coma and death. History and diagnosis by Dr. P., private physician. Necropsy unsatistactory because of post-mortem decomposition. Examination of intestinal contents positive for cholera vibrios.

Case 7.—A. V.—Age, 4 years. Female. Diagnosis, chronic enteritis. Duration of illness, six months. No symptoms of cholera. Diagnosis and history by Dr. H., municipal physician. Specimen taken from intestine at post-mortem examination positive for cholera vibrios.

Case 8.—C. F.—Age, 5 years. Female. Diagnosis, acute dysentery. Bloody stools. Duration of illness, eight days. No symptoms of cholera. History and diagnosis by Dr. Q., private physician. Specimen taken from intestinal contents positive for cholera vibrios.

Case 9.—S. A.—Age, 2 years. Female. Acute meningitis. History and diagnosis by Dr. H., private physician. Taken sick, September 15, with fever and nausea. Vomited a worm. Stool contained other worms. September 16 had two liquid stools. September 17, no stools, very restless, side to side movements of the head. September 18 and 19 the same condition with some delirium. September 20, fever, 39.5° C., general convulsions, photophobia. Purgative and ice cap prescribed. One large stool. Condition unimproved. Died at 11 p. m.

Necropsy twenty-seven hours after death by Doctor Andrews.

Body well nourished, rigor mortis slight, nails blue, eyes sunken and lids half closed.

Subcutaneous tissues dry, muscles dark.

Peritoneum dry, smooth, no fluid in cavity.

Pericardial sac contains few drops of fluid. Right side of heart soft, left, firm.

Lungs.—Organs crepitate throughout, light pinkish gray in color. Cut section, dark cherry surface from which dark tarry blood can be expressed.

Kidneys soft, light plum colored, capsule strips readily, striations seen clearly. Cortex a dull gray color.

Intestines congested in some parts, the congestion being more marked in lower part of ileum. Contents semifluid, yellow color. Mucosa intact. Intestines distended with gas.

Urinary bladder empty.

Brain.—Meninges congested, dry, brain substance firm, vessels in brain substance also congested. No fluid in ventricles. No evidence of inflammation.

The intestinal contents were examined bacteriologically by the Biological Laboratory, Bureau of Science, and a diagnosis of cholera made.

Case 10.—M. S.—Age, 2 years 4 months. Female. Said to have had slight fever September 9. September 19, had watery stools of a fæculent character. Family stated that diarrhœa continued until death. Dr. R., private physician, furnished the following history: Called on September 20 to what he considered case of acute meningitis; he prescribed calomel and rhubarb and castor oil. He noted high fever, 39° C., strabismus, rigidity of neck, restlessness, and evidences of headache. The urinary secretion was present.

Necropsy fourteen hours after death by Doctor Andrews.

Body well nourished, rigor mortis absent, nails blue, skin shrunken, eyes half open.

Subcutaneous tissues dry.

Peritoneal cavity slightly moist, contains no fluid.

Pericardial sac contains few drops of fluid. Right side of heart distended with blood, left side firm.

Lungs.—Left voluminous, crepitant. Cut section, reddish-brown from which a frothy blood-tinged fluid can be expressed. Right lung similar, slight increase of pleural fluid in both cavities.

Kidneys.—Fœtal lobulations obliterated, capsule strips easily. Cut section, cortex and medulary portion dull gray in color, striations indistinct.

Urinary bladder contains about 30 cubic centimeters of pale turbid urine.

Brain.—Meninges of brain are deeply congested, otherwise apparently normal. Slight amount of blood-tinged fluid in lateral ventricles; blood vessels are engorged.

Intestines distended with gas, slightly congested, mucosa intact throughout. Contain semi-fluid, brownish yellow fluid, slight in amount. Solitary lymph follicles slightly enlarged, especially in the lower end of the ileum. Peyer's patches are not involved except those immediately above the ileo-cæcal valve.

Examination of intestinal contents reported positive for cholera by the Biological Laboratory, Bureau of Science.

Case 11.—T. N.—Age, 10 months. Female. History and diagnosis of acute meningitis by Dr. B. Taken sick on September 14 with fever. September 15, two bowel movements of yellow color. September 16, temperature 38° C., nausea, strabismus and evidence of headache. Calomel prescribed. September 17, no bowel movements. September 18, temperature normal, strabismus and general convulsions. September 19, same. September 20, 21 and 24, adynamic and semi-comatose condition. Died at 3 p. m. September 22.

Necropsy by Doctor Andrews:

Body of small infant, rigor mortis absent, nails bluish. Skin shriveled, expression of face drawn; eyes sunken, half open.

Subcutaneous tissues and muscles dry.

Peritoneum moist but no fluid in cavity.

Pericardial sac contains a few drops of fluid. Right side of heart distended, left side firm.

Lungs.—Left voluminous, heavy, light purple in color. Posterior part of lower lobe has a slight consolidation present. Cut section of the lower lobe shows a dark cherry surface in which two or three dark slightly elevated areas are seen. These are drier than the surrounding tissues and more granular. Right lung, dark gray anteriorly, dark purple posteriorly. Posterior border firmer than anterior part. Lung is voluminous, slight amount of frothy material can be expressed.

Kidneys are soft, fœtal lobulations absent, surface grayish purple in color. Cut section shows cortex and medullary portion to be of a dull gray color. Striations indistinct.

Urinary bladder empty.

Brain.—Meninges are very much congested. Basal part of brain shows considerable congestion with slight increase of spinal fluid. No inflammatory exudate present. Choroid plexus in lateral ventricles much congested. No fluid present. Section of brain shows intense congestion throughout its substance.

Examination of intestinal contents reported positive for cholera by the Biological Laboratory, Bureau of Science.

Case 12.—T. G.—Age, 3 years. Female. History by Medical Inspector A. Diagnosis, acute meningitis by Dr. R., private physician. September 22, had 4 liquid stools without fever or vomiting. September 23, no bowel movements. September 24, calomel and castor oil administered by Dr. R. Slight fever and convulsions. Semi-comatose, dyspnœa and death at 4 p. m.

Necropsy by Doctor Andrews.

Body slightly emaciated, rigor mortis absent. Nails blue, skin shriveled; expression drawn; eyes half open and sunken.

Subcutaneous tissues fairly dry.

Peritoneum moist, fluid absent.

Pericardial sac contains several drops of fluid. Heart is very soft.

Lungs voluminous, crepitant. Cut section shows congestion, dark tarry blood can be expressed.

Kidneys soft, grayish red in color, capsule strips readily, fœtal lobulations absent. Cut section shows grayish red surface in which the medullary portion and the cortex show clearly with the striations partially obliterated.

Intestines slightly congested, filled with watery material mixed with mucus and dark fæcal material.

Urinary bladder empty.

Examination of intestinal contents reported positive for cholera by Biological Laboratory, Bureau of Science.

Case 13.—E. M.—Age, 1 year. Female. History and diagnosis of chronic enteritis by Dr. G., municipal physician. Indefinite history of malnutrition and digestive disturbance, fever, constipation and diarrhœa alternating. Presented picture of marasmus. On September 21, removed to 192 Calle Felix Huertas where a case of cholera had occurred the previous day. No symptoms of cholera present; patient died four days later (September 25).

Necropsy by Doctor Andrews.

Body greatly emaciated, rigor mortis absent, nails white, skin not shriveled, no external evidence of cholera.

Subcutaneous tissues moist.

Peritoneum moist, few cubic centimeters of fluid present.

Pericardial sac grayish white. Heart is soft.

Lung.—Voluminous, pinkish gray in color, lower lobe of left lung firm, solid, slight fibrinous exudate on its surface. Cut section shows hepatization, grayish brown in color, quite moist. Upper lobe crepitant. Cut section pinkish in color. Right lung upper lobe dark red, firm, numerous petechial hæmorrhages show beneath visceral pleura. Cut section shows hepatization, surface light brown in color, and is moist. Pieces sink in water. Lower lobe softer than upper, dark colored, similar in consistency.

Spleen.—Enlarged, firm, dark purple. Cut section shows dark chocolate surface in which Malpighian bodies and trabeculae are seen plainly.

Kidneys.—Left is enlarged, fœtal lobulations lost, pale gray in color, capsules strip readily. Cut section shows moist surface, anæmia. Striations clearly seen, glomeruli seen as reflecting dots of light.

Liver enlarged, chocolate colored, lobulations distinct. Organ fairly firm.

Intestines not congested, mucosa intact, contents are watery with some yellowish semi-fluid fœcal material.

Urinary bladder empty.

Examination of intestinal contents reported positive for cholera by the Biological Laboratory, Bureau of Science.

Case 14.—L. S.—Age, 1 month 29 days. Male. History and diagnosis by Dr. C., municipal physician. September 16 had fever, vomited milk; abdomen was distended. September 17, fever, slight strabismus, no diarrhœa, thirst, and in a semicomatose condition. September 18, fever higher, "localized in the head," cold extremities, transient convergent strabismus, much restlessness, crying continually. Diagnosis, acute meningitis.

The medical inspector in charge of the district failed to secure a sample of the intestinal contents of the child.

Case 15.—L. S.—Age, 3 years. Brother of case 14. Taken sick on September 13 with vomiting and diarrhœa. Three to five movements per day. Stools were fæculent and fœtid. Thirst, no loss of voice, and no suppression of urine. Fever first two days, but afterwards temperature normal.

Necropsy by Doctor Andrews.

Body well nourished, rigor mortis marked; nails blue; skin shriveled; eyes half open and sunken.

Subcutaneous tissues moist, muscles dark.

Peritoneum smooth and moist, few cubic centimeters of blood-colored fluid present. Intestines distended with gas, slightly congested.

Pericardial sac blood-stained, increase of fluid. Heart soft, flabby and blood-stained.

Lungs.—Increase of pleural fluid in both cavities. Lungs voluminous and heavy. Cut section shows congestion and considerable frothy fluid present.

Kidneys swollen, soft, capsule strips readily. Cut section dull gray color. Striations partially obliterated. Intestines distended with gas. Lower part of ileum slightly congested, contents dark and watery; mucosa intact.

Urinary bladder contains about 200 cubic centimeters of dark colored urine.

Examination of intestinal contents for cholera reported positive by the Biological Laboratory, Bureau of Science.

It seemed probable at first glance that cases of cholera were being concealed, or that typical symptoms were carelessly overlooked, but I have seen a number of cases in which a diagnosis of Asiatic cholera would not have been made from the clinical picture; and without the bacteriological investigation of the stools these cases would never have been recognized as cholera. I am convinced that many of the diagnoses of acute or chonic enteritis, acute dysentery, meningitis, etc., are made in good faith by the Filipino doctors. They have erred in looking for a typical picture of Asiatic cholera, and this picture is lacking in children in many instances. The erroneous diagnosis of chronic and acute enteritis and of dysentery alone is often due to the actual presence of these conditions, probably before infection with cholera occurred, and to the absence of the classical symptoms of cholera.

The frequency of diagnosis of meningitis by native phycisians is due to lack of or failure to observe the early symptoms of cholera, vomiting, rice-water diarrhœa, muscular cramps, collapse and anuria, and to the presence, late in the disease, of marked cerebral symptoms, due to a profound toxæmia. Accurate diagnosis of cholera in these fatal cases was only possible from the post-mortem findings and the isolation of cholera vibrios from the intestines.

In other cases, we have found the acute enteritis, acute parenchymatous nephritis, dryness of the tissues and serous cavities, tarry appearance of the blood on section of the lungs, dry appearance of the spleen on cut section, and other pathological appearances of cholera, without being able to demonstrate the presence of cholera vibrios in the intestines. These cases were probably cholera in which the duration of the illness was so long that the disappearance of the vibrios from the intestines had occurred.

The following diagnoses were made by municipal physicians and private physicians, apparently acting in good faith. An effort was made to investigate cases of acute intestinal troubles in living children, and a circular letter was addressed to all practicing physicians in Manila requesting samples of the dejections of children ill with enteritis, dysentery and allied disorders. Municipal physicians and medical inspectors were directed to secure such samples wherever possible. The medical profession was apathetic and but few physicians, responded. The municipal physicians and the medical inspectors, however secured a considerable number of samples, and of these several with very atypical symptoms were found to be positive for cholera organisms as described below.

LIVING CASES.

Case 16.—I. M.—Age, three months. Male. Slight diarrhœa; mother stated that child had vomited. Seen in convulsions. Admitted to San Lazaro Hospital September 9. Temperature normal. This case may be regarded as an example of what is commonly diagnosed as acute meningitis in Manila. It presented symptoms of cortical irritation, twitching and convulsive movements; some apparent but not real rigidity of the neck, and spasmodic movement of the head from side to side. After admission to the hospital, no vomiting or diarrhœa occurred; the stools were soft and fæculent. There was no collapse and no anuria. The urine was highly albuminous, and during the following ten days the temperature was always normal or slightly elevated. Examination of the intestinal contents revealed the presence of the cholera vibrio, and this organism remained present for ten days as was demonstrated by daily bacteriological examination. The patient recovered.

Case 17.—P. M.—Age, 5 years. Male. A diagnosis of acute dysentery and meningitis was made by a municipal physician. Duration of illness, one week. Blood and mucus in stools. No vomiting or other symptoms of cholera. Admitted to San Lazaro Hospital on September 14. Had cerebral symptoms, twitching, rigidity of muscles of neck, head drawn back, urine scanty and highly albuminous. Examination of the intestinal contents positive for cholera vibrios. The urine increased in quantity, the cerebral symptoms disappeared, the vibrios disappeared from the intestines, and the patient was discharged cured on September 21.

Case 18.—E. P.—Age, 4 years. Female. Duration of illness, fifteen days. Fever but no vomiting. Diarrhœa, alternating with constipation was present. The patient was treated for worms and later for meningitis by Dr. G., municipal physician. Admitted to San Lazaro Hospital September 16. No symptoms of cholera. Temperature 100.4 on entrance. The temperature reached normal on the next day and remained normal until recovery. Cerebral symptoms, muscular twitchings and convulsive movements were present. The patient was semi-comatose at times. There was no anuria. The urine was albuminous. The cerebral symptoms disappeared within twenty-four hours after admission to the hospital. Examination of the intestinal contents was positive for the cholera spirillum. The patient was discharged cured, September 20.

Case 19.—M. M.—Age, 1 year 7 months. Male. September 20, had fever; two liquid stools, no vomiting, slight meteorism. September 21 and 22, two stools per day, of a yellow color. Semi-comatose at times. Diagnosis, acute enteritis. History and diagnosis by Dr. G., municipal physician. Admitted to San Lazaro Hospital on September 23. Pulse, good; respiration, good. Large

liquid stool at 7 p. m. Slept well. Passed roundworm. September 24, yellow liquid stool, face flushed, pulse full, respiration somewhat labored, voiding of urine normal. Did not retain nourishment. September 25, slight rigidity of muscles of neck, patient insists on lying on back. Sleeps better, apparently recovering. Examination of intestinal contents positive for cholera spirillum.

Case 20.—R. V.—Age, 1 year 4 months. Female. Duration of illness at time of admission to hospital, five hours. Mother stricken with cholera the day before. Admitted to hospital September 19. Condition upon admission apparently fair. Temperature 102, pulse 140, respirations 55. An enema was administered and when passed small flakes and guava seeds were present. Voiding of urine normal. Abdomen greatly distended on the evening of the 19th. Patient frequently vomited nourishment. The temperature varied between 102° and 99.4° but registered 103.6° on September 25 at 5 p. m. The stools as a rule were greenish and liquid. Stool specimen of September 19 was positive for the cholera vibrio. The patient recovered.

Case 21.—F. M.—Age, 1 year 3 months. Male. History and diagnosis of acute enteritis by Dr. G., municipal physician. September 21 had yellow stools. No fever. September 22, slight diarrhœa continued; no fever. September 23 and 24, child much better. September 25, one soft yellow stool; sample from this was positive for cholera vibrios. Admitted to San Lazaro Hospital September 26, at 10.50 a. m. No symptoms. Child apparently well. Held awaiting disappearance of vibrios from intestinal tract.

Case 22.—M. B.—Age, 1 year 4 months. Female. History by Dr. B., medical inspector, Bureau of Health. September 21, diarrhœa and passing of worms. Stomach distended, also vomited a roundworm. Dr. R. was called and diagnosed acute gastro-enteritis. Specimen was taken and the Bureau of Science reported positive for cholera. Dr. B. noted the following: Eyes slightly sunken, lids slightly drooping; fitful and restless; very slight wrinkling of skin of fingers and toes; abdomen distended; diarrhœa had ceased, pulse rapid, temperature normal, body warm, urine not suppressed. Admitted to San Lazaro Hospital September 24, 9.45 a. m.

On admission, patient's condition was fairly good; irritable all afternoon of 24th; stools liquid; temperature varies from 98.6° to 100.2°. Voids urine freely. September 25, temperature 99.8°, pulse 144, respiration 28. Pulse intermittent. September 27, quiet, slept most of night. Temperature 98.4°, pulse 102. General condition practically normal.

The average number of deaths from enteritis, meningitis and dysentery during months in which cholera is not reported in Manila varies about as follows:

	Cases per month.
Enteritis	40– 50
Meningitis	20– 30
Dysentery	10– 20
Total	70–100

This is the death rate which may be expected when cholera is not present officially. By examination of the tables, it will be noted that whenever cholera is present the increase in the number of cases of enteritis, dysentery and meningitis is remarkable; so that one may say that if the total for these three diseases exceeds 100 cases per month there is probably cholera in Manila. (See Table IV.)

Sufficient work has already been done to show that many cases of cholera in children during epidemics are unrecognized and unreported as such. Further, careful investigation of all acute diseases and of deaths of children during inter-epidemic periods is necessary before an opinion can be expressed upon the possibility of cholera existing in Manila unreported for months. This work will be carried out as rapidly as possible and I hope before long to be able to present additional interesting data upon the actual findings in cases reported as "infantile" beriberi, convulsions of children, acute bronchitis and other diseases of children.

There were two cases of cholera reported in July but the epidemic can be said to have commenced August 17 with two cases in Bancusay. From August 17 to date, September 25, there has been a total of 83 cases. To accentuate the importance of the examination of the stools of children reported as suffering with other diseases, I need only call attention to the fact that 27.7 per cent of the total cholera cases were reported as victims of other diseases, and that without routine stool examinations they would never have been recognized as cholera.

CONCLUSIONS.

Cholera in children is often unrecognized and unreported as such, being reported as acute or chronic enteritis, gastro-enteritis, entero-colitis, dysentery, acute or simple meningitis, and probably also as "infantile" beriberi, convulsions of children, and other diseases.

The occurrence of these errors in Manila makes it more than probable that the same confusion exists in a greater degree in the provinces, where skilled diagnosticians are more rarely found.

The clinical picture of cholera in children is often atypical, and the diagnosis may be extremely difficult if not impossible without a bacteriological examination of the intestinal contents. Cerebral manifestations in children suffering from cholera are very common, and their severity is in inverse proportion to the age of the child. Acute meningitis is a very rare disease in Manila, in spite of the statistics to the contrary. The percentage of children attacked by cholera is higher than shown by the statistics of the Bureau of Health.

Further investigation is necessary to demonstrate the relation between "infantile beriberi," "acute bronchitis," "convulsions of children," etc., and cholera in children.

During cholera outbreaks and during June, July and August and September, all acute diseases of children should be reported to the Bureau of Health. A bacteriological investigation of the intestinal contents should be made in every case.

ILLUSTRATIONS.

Charts 1 to 6.

TABLE I.—*Deaths from cholera and meningitis in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Meningitis.	Cholera.	Meningitis.	Cholera.	Meningitis.
January		23	151	78		33
February		23	11	92	1	32
March		22	5	44		34
April		28		31		27
May		37	1	35		24
June		23	3	45		48
July	2	27	14	93	2	31
August	5	34	48	64	5	40
September	64	53	396	62		
October	65	58	137	54		
November	32	43	30	46		
December	26	50	7	45		

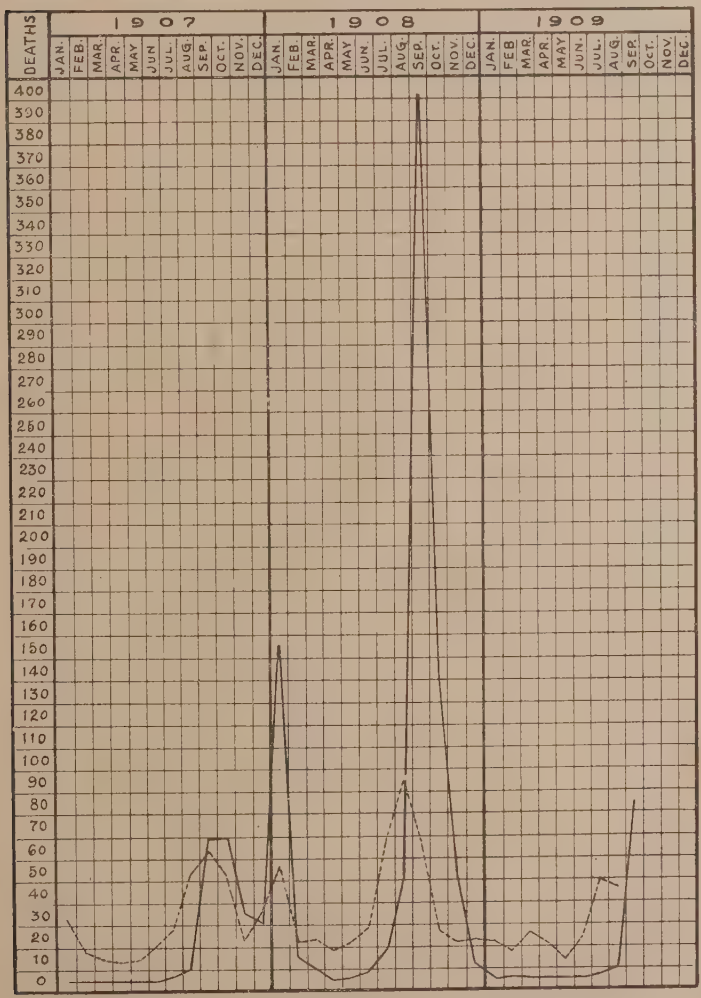


FIG. 1.—Monthly fluctuations of the number of deaths from cholera (solid line) compared with those from meningitis (dotted line).

TABLE II.—*Deaths from cholera and enteritis in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Enteritis.	Cholera.	Enteritis.	Cholera.	Enteritis.
January		50	151	63		33
February		35	11	42	1	25
March		37	5	45		44
April		49		43		29
May		40	1	37		58
June		53	3	73		81
July	2	81	14	163	2	120
August	5	118	48	144	5	103
September	64	103	396	110		
October	65	60	137	52		
November	32	41	46	28		
December	26	58	7	38		

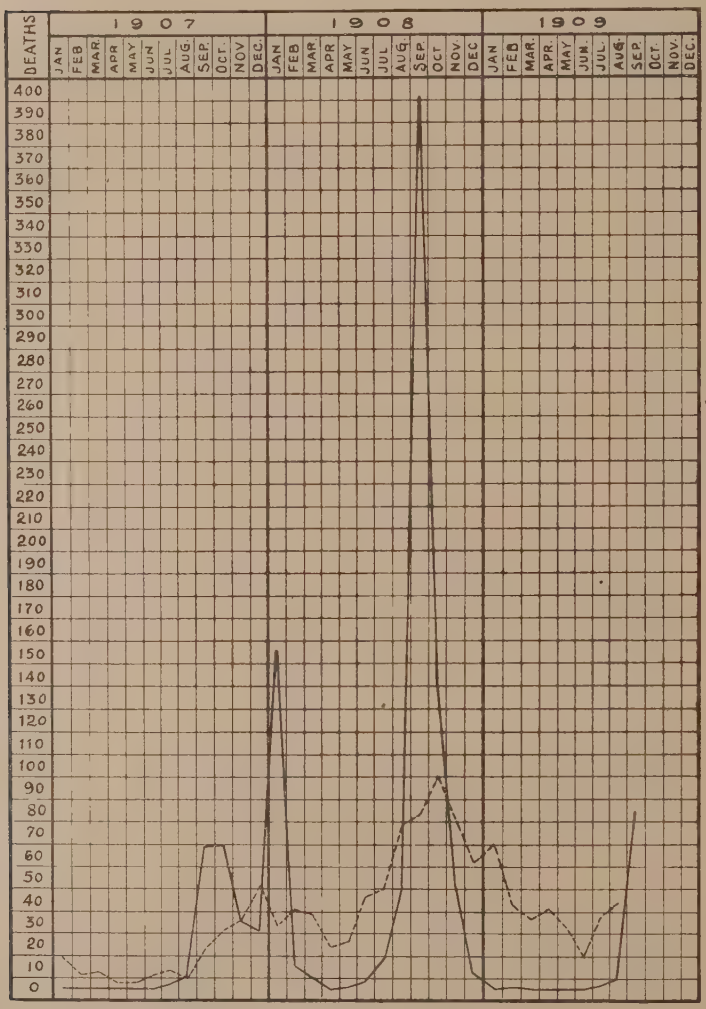


FIG. 2.—Monthly fluctuations of the number of deaths from cholera (solid line) compared with those from enteritis (dotted line).

TABLE III.—*Deaths from cholera and dysentery in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Dysentery.	Cholera.	Dysentery.	Cholera.	Dysentery.
January		28	151	52		17
February		13	11	18		13
March		10	5	19		21
April		9		14		16
May		10	1	17		9
June		16	3	24		19
July	2	23	14	61	2	45
August	5	49	48	90	5	31
September	64	59	396	63		
October	65	47	137	23		
November	32	18	46	17		
December	26	31	7	18		

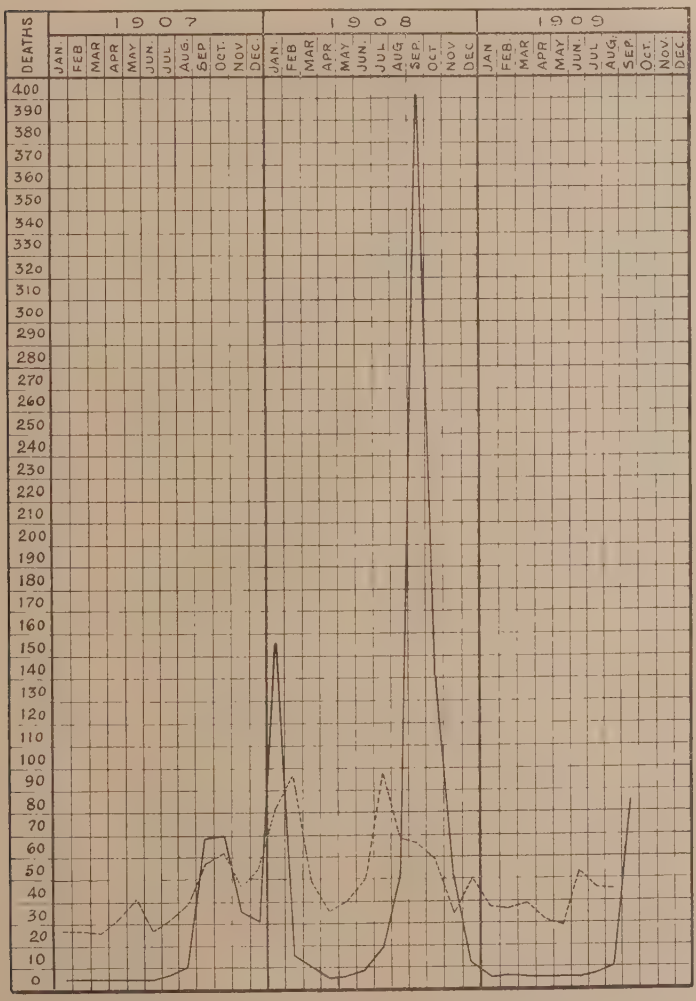


FIG. 3.—Monthly fluctuations of the number of deaths from cholera (solid line) compared with those from dysentery (dotted line).

TABLE IV.—*Deaths from cholera and meningitis, enteritis and dysentery combined in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Enteritis, dysentery, and meningitis.	Cholera.	Enteritis, dysentery, and meningitis.	Cholera.	Enteritis, dysentery, and meningitis.
January		101	151	193		83
February		71	11	152	1	70
March		69	5	108		101
April		86		88		73
May		87	1	89		91
June		92	3	142		148
July	2	131	14	320	2	196
August	5	201	48	298	5	174
September	64	215	396	235		
October	65	165	137	129		
November	32	102	46	75		
December	26	139	7	101		

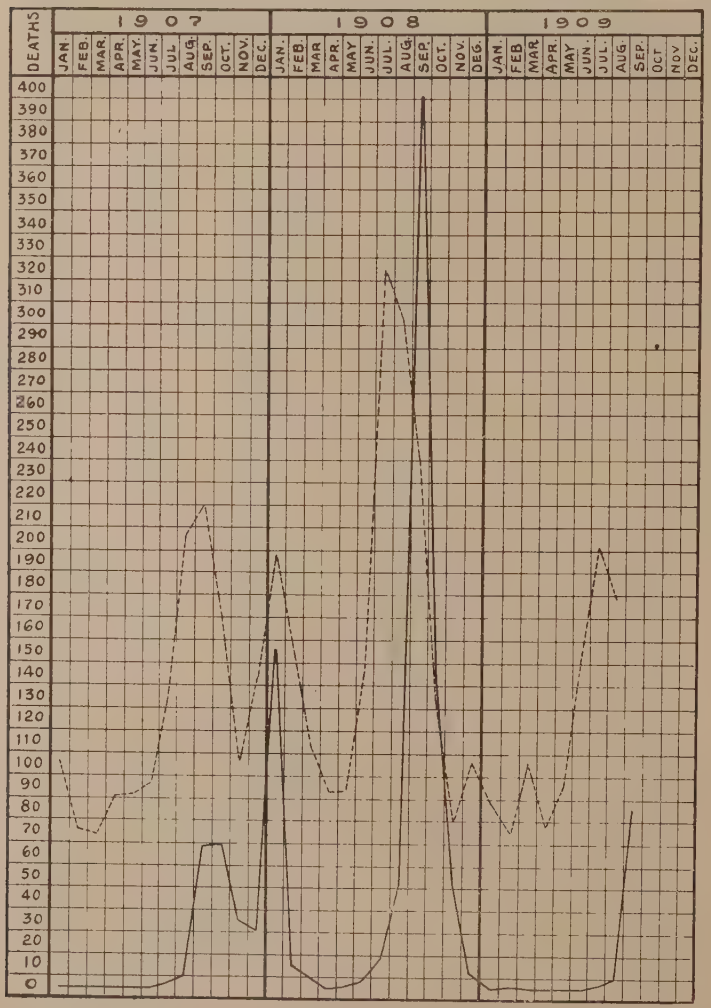


FIG. 4.—Monthly fluctuations of the number of deaths from cholera (solid line) compared with those from meningitis, enteritis and dysentery combined (dotted line).

TABLE V.—*Deaths from cholera and "infantile" beriberi in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Infantile beriberi.	Cholera.	Infantile beriberi.	Cholera.	Infantile beriberi.
January		14	151	29		65
February		6	11	36	1	38
March		8	5	34		12
April		3		19		36
May		3	1	22		28
June		6	3	41		15
July	2	9	14	45	2	33
August	5	5	48	74	5	39
September	64	18	396	18		
October	65	26	137	95		
November	32	32	46	76		
December	26	46	7	57		

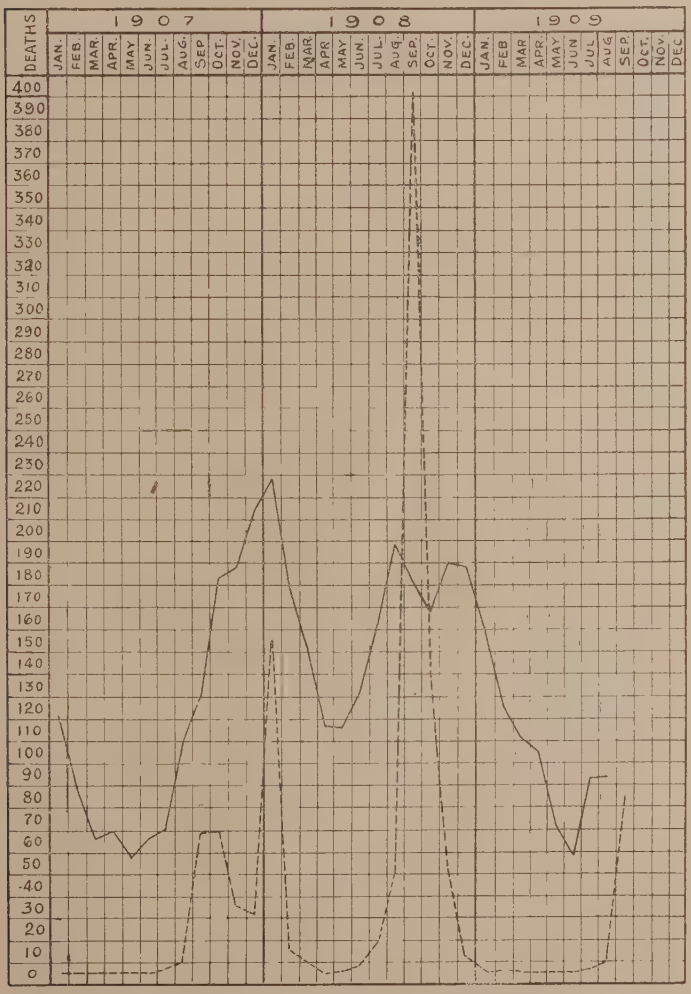


FIG. 5.—Monthly fluctuations of the number of deaths from cholera (solid line) compared with those from "infantile" beriberi (dotted line).

TABLE VI.—*Deaths from cholera and infantile convulsions in Manila.*

Month.	1907.		1908.		1909.	
	Cholera.	Infantile convulsions.	Cholera.	Infantile convulsions.	Cholera.	Infantile convulsions.
January		117	151	223		156
February		84	11	173	1	120
March		61	5	146		106
April		65		112		100
May		53	1	111		67
June		61	3	127		54
July	2	66	14	158	2	88
August	5	105	48	193	5	89
September	64	125	396	177		
October	65	178	137	164		
November	32	183	46	185		
December	26	209	7	183		

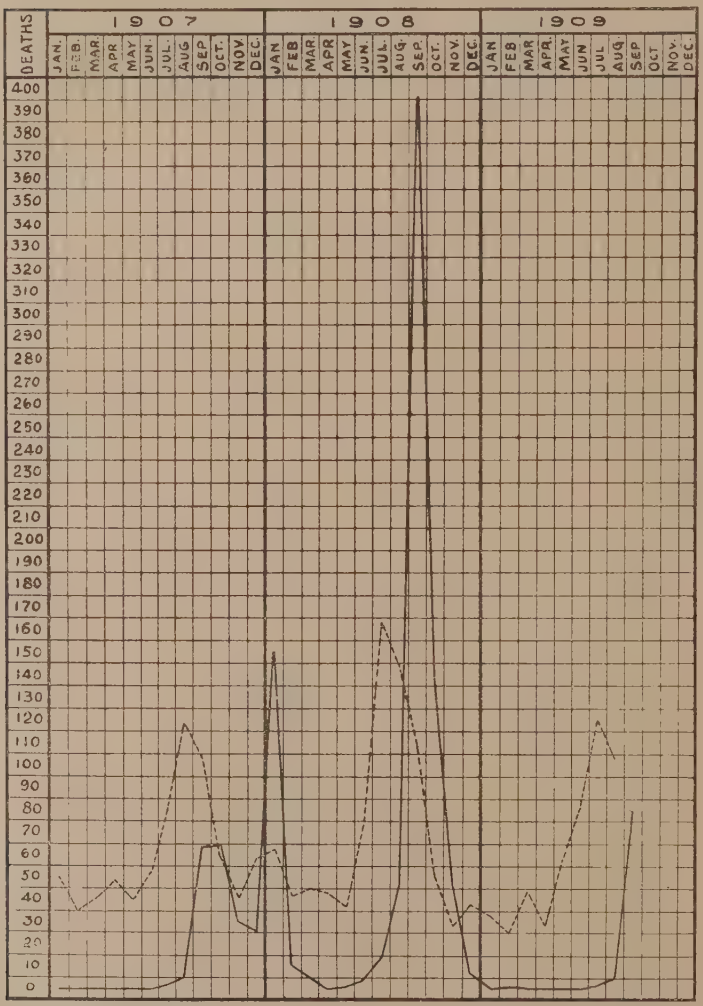


FIG. 6.—Monthly fluctuations of the number of deaths from cholera (dotted line) compared with those from infantile convulsions (solid line).

OBSERVATIONS ON CATTLE PLAGUE IN THE PHILIPPINE ISLANDS AND THE METHODS EMPLOYED IN COMBATING IT.

By E. H. Ruediger.

(*From the Serum Section of the Biological Laboratory, Bureau of Science*).

A great deal has been written on the subject of cattle plague [1] and the literature is so voluminous that I shall not attempt to review it at this time. All I shall aim to do is to give a brief outline of the more important features of the disease as observed in these Islands and the method employed in combating it here.

Cattle plague is an acute infectious disease characterized by rapid rise of temperature, severe prostration, loss of appetite, hyperæmia of the conjunctivæ, discharge from the nose, violent diarrhœa, and, in the majority of cases, death. The disease is endemic and epidemic, especially in the warmer countries such as China, India, Egypt, other parts of Africa and the Philippine Islands. Many attempts to cultivate and isolate the causative factor have resulted in failure. A number of authors maintain that the organism is ultra-microscopic because it passes through porcelain filters. So far as my own experience with filtered blood is concerned, I feel safe in saying that the filtrate is absolutely harmless when injected into non-immune animals. At any rate, the infectious material present in the blood does not pass through either the Chamberland or the Berkefeld filters.

MODE OF INFECTION.

While the causative factor of cattle plague is as yet unknown, it is generally accepted that infection is conveyed by discharges from a sick animal. Pastures that have been infected by sick animals may remain infected for months or even for years. At times the weather appears to have an influence on the disease. In the Philippine Islands cattle plague nearly disappears during the dry season only to spring up in widespread epidemics soon after the beginning of the rainy season. Cattle kept on high land usually suffer less than those kept on low land. Infected stables, unless well cleaned and disinfected, will remain infectious for a long time. Non-immune animals kept in the vicinity of sick animals

[1] German, *rinderpest;* French, *peste bovine.*

but not coming in actual contact with the latter, may become infected either through attendants who have been in contact with the sick animals, or by the feed or utensils soiled with discharges from them; and the infection may be carried also by birds or flies which eat freely of excreta from the sick animals and then share the food of well animals. Surface water draining from sick toward non-immune animals is sure to carry with it infectious matter. Healthy animals may be infected artificially by mixing discharges from sick ones with the food or water, by directly rubbing discharges into the mouth and nose, or by injecting subcutaneously discharges or blood from a sick animal. After infection has taken place, there is an incubation period varying from two to seven days, rarely longer, before sypmtoms appear.

SYMPTOMS.

In these Islands the disease is usually ushered in by a rapid rise of temperature, the temperature rising 2° or 3° C. within twelve hours. The conjunctivæ are greatly reddened and there is a watery discharge from the eyes and a more or less viscid discharge from the nose. Prostration is severe and there is loss of appetite. Diarrhœa sets in on the third or fourth day after the initial rise of temperature. The animal soon passes blood, mucus and portions of the intestinal mucosa, and on about the sixth or seventh day the temperature usually drops rapidly and the animal dies in collapse.

MORBID ANATOMY.

The pathologic lesions vary from discrete ulcers in the stomach and intestines to complete shedding of the mucosa. I have even seen animals pass pieces of intestinal mucosa measuring a meter or so in length, and at autopsy one frequently finds the mucosa completely separated from the remainder of the intestine, ready to be passed off. A large quantity of blood is found in the intestines in such cases. The solid viscera show more or less parenchymatous change. There is no enlargement of the spleen. The mesenteric and other lymph glands are enlarged and hyperæmic.

DIFFERENT FORMS OF CATTLE PLAGUE.

In cattle plague, as in many other diseases, one scarcely ever sees two cases which are alike in all respects, and, for sake of convenience, I will divide the disease as it has come under my observation in the Philippine Islands into the following four forms: Common form, very acute form, afebrile form, and the constipated form.

Common form.—In the common form of cattle plague the temperature rises rapidly, there is discharge from the nose and eyes with reddening of the conjunctivæ, and marked prostration. Diarrhœa sets in on the second or third day, the fæces become bloody and the animal dies in about seven

days. At autopsy one finds extensive ulcerations in the mucosa of the stomach and intestines, with occasional shedding of portions of the mucous membrane.

Very acute form.—This form of cattle plague runs a very rapid course. An animal may be apparently well in the evening and be found dead the next morning. Behind the animal a pool of liquid fæces is found with blood and pieces of intestinal mucosa. There is profuse hæmorrhage into the intestines. It would seem that the mucosa is dissected from the underlying tissue by submucous hæmorrhage.

Afebrile form.—Occassionally one sees an animal which appears not to be well, yet has no temperature sufficient to arouse suspicion of cattle plague. The animal loses appetite, has a slight diarrhœa and gradually wastes away in two or three weeks. At autopsy one finds moderate gastro-enteritis without ulceration.

Constipated form.—Although this is a very rare form of the disease, yet in a few instances cattle plague with constipation has been observed. There is rapid rise of temperature, loss of appetite and severe prostration. Death results in four or five days and at autopsy one finds extensive ulcerations limited to the stomach.

ASSOCIATION WITH OTHER DISEASES.

Of the diseases appearing with cattle plague, foot-and-mouth disease occurs most frequently in the Philippine Islands. Although foot-and-mouth disease in itself is not very serious in these Islands, yet when it occurs simultaneously in an animal with cattle plague, the combination proves fatal in nearly every case in spite of the best care and treatment. Other diseases encountered in the Philippine Islands in connection with cattle plague are Texas fever and surra, both of which are very destructive to life.

DIAGNOSIS.

As a rule the diagnosis presents no difficulties, especially in localities frequented by epidemics of the disease. Rapid rise of temperature, loss of appetite, prostration, reddening of the conjunctivæ, discharge from the eyes and nose and diarrhœa are sufficient, when present, to warrant a diagnosis of cattle plague. During an epidemic, sudden rise of temperature alone should justify the diagnosis, for it is of the utmost importance to begin treatment early if the animal is to be treated at all.

PROGNOSIS.

Cattle plague is very destructive to life. Even in localities where it is endemic it may destroy 70 to 80 per cent of the animals attacked. Recovery seems more likely to occur among the younger animals than among the older ones. Ninety-five to 100 per cent of animals from a country entirely free from cattle plague die if brought into contact with the disease.

TREATMENT.

Little or nothing can be accomplished with drugs. The administration of specific immune serum gives good results where treatment is begun early enough. The serum is prepared by hyper-immunizing cattle against the disease. This is accomplished as follows: Blood of an animal sick with cattle plague transmits the disease when injected under the skin of a non-immune animal. If compelled to start without a curative serum, an animal which has spontaneously recovered from the disease is given an injection of 100 cubic centimeters of virulent blood (blood of an animal suffering from an acute form of the disease) under the skin. Within a few days the animal usually sickens, with a slight rise of temperature from which it soon recovers. Having recovered from the effects of the inoculation, the animal receives a larger quantity of virulent blood, and these treatments are repeated until at least 1,000 cubic centimeters have been given at one dose. The process of immunization should not require more than three months' time, and an animal so treated usually furnishes a good protective serum. Once in possession of immune serum, any animal may be immunized by injecting serum and virulent blood simultaneously. Usually from about 50 to 100 cubic centimeters of specific serum are injected under the skin on one side of the animal and from 0.5 cubic centimeter to 1 cubic centimeter of virulent blood under the skin on the other side of the animal. Within a week the animal sickens and goes through a mild attack of cattle plague. Should the temperature rise very high, 41° C. or over, serum treatment should be resorted to. After recovery from an attack of the disease, there is practically no danger of killing the animal by injecting virulent blood. A dose of 500 cubic centimeters may be given without hesitation. The following may be considered a safe procedure in immunizing an animal for curative serum. From about 50 to 100 cubic centimeters (according to the size of the animal and the potency of the serum) of immune serum and from 0.5 cubic centimeter to 1 cubic centimeter of virulent blood are injected simultaneously. I do not fix a rule regarding the exact quantity of immune serum an animal undergoing immunization should receive. Here in the Philippine Islands we have to deal with cattle from China, from India, and from Australia, and with both cattle and carabaos from various parts of the Philippine Islands, some of which are highly susceptible, others but moderately so, others show a considerable degree of insusceptibility, while still others are entirely immune. To be conservative and economical is the best advice I can give.

After the animals have recovered from the first reaction, the following quantities of virulent blood may subsequently be injected: 250, 500, 750 and 1,000 cubic centimeters. Larger doses of virulent blood such as 500, 1,000, 2,000 and 4,000 cubic centimeters may also be given. From seven to ten days after recovery from the effects of the last inoculation

the animal is bled three times at intervals of one week. A few days after the third bleeding, the animal is again inoculated with virulent blood, this time one large dose being given, and then bled again three times. This inoculating and bleeding might be continued for years, but, as a rule, the animal is sold after the third series of bleedings, having been bled nine times in all. The blood is collected in sterile flasks or cylinders and allowed to clot, and as the serum separates from the clot it is poured into a sterile vessel. A small quantity of phenol is then added to the serum, after which the serum is passed through a germ-proof filter and is bottled for use.

USE OF ANTICATTLE-PLAGUE SERUM.

The immune serum may be used as a curative agent in animals already infected or it may be used as a preventative. Little or nothing can be accomplished with serum during a virulent attack of cattle plague unless the treatment is begun early. The experience of others and of my self proves that animals which have been sick with the disease for three, four or five days can no longer be saved. Chart No. 1 shows the temperature curve of an animal in which the serum treatment was begun on about the sixth day. I doubt whether life was prolonged even in this case.

Serum treatment begun on the third day of the disease appears to have no effect on the temperature curve nor on the course of the disease. (Chart No. 2.) Even a severe attack of the disease may be brought to a favorable termination when treatment is begun on the first day and when large doses of serum are given. (Chart No. 3.) Protective measures by means of immune serum in experienced hands give far more satisfactory results. The injection of serum alone confers a temporary immunity only, perhaps for not longer than two or three months and hence this method can not be recommended for general purposes other than of temporarily checking an epidemic of cattle plague. In order to accomplish the desired result, the simultaneous method of inoculation must be resorted to as follows: A small quantity of virulent blood is injected under the skin of the animal to be immunized and at the same time an appropriate dose of immune serum is given in some other part of the body. Within a week after inoculation the animal, if susceptible, becomes sick and experiences a mild attack of cattle plague; after which it may be considered immune throughout life. Should the temperature rise high during the reaction, more serum should be given. One-half cubic centimeter of virulent blood suffices for the first inoculation. Even in animals which have received this small quantity of virulent blood, curative measures are frequently resorted to early in the reaction if the temperature rises high. (Chart No. 4.) One cubic centimeter of virulent blood may be given with good result. (Chart No. 5.) After an inoculation with 5 cubic centimeters of virulent blood, the reaction

appears to be more severe and larger doses of serum may be required to save the life of the animal. (Chart. No. 6.)

Although the accompanying charts show a more severe reaction after the larger dose of virulent blood, the severity may have been due to other causes, such as individual susceptibility of the animals, difference in the potency of the serum or difference in the virulence of the blood employed.

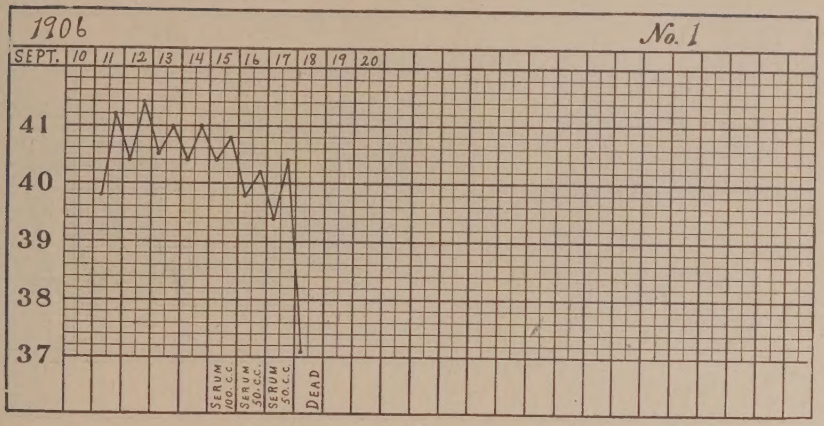
MANAGEMENT OF THE SERUM STATION.

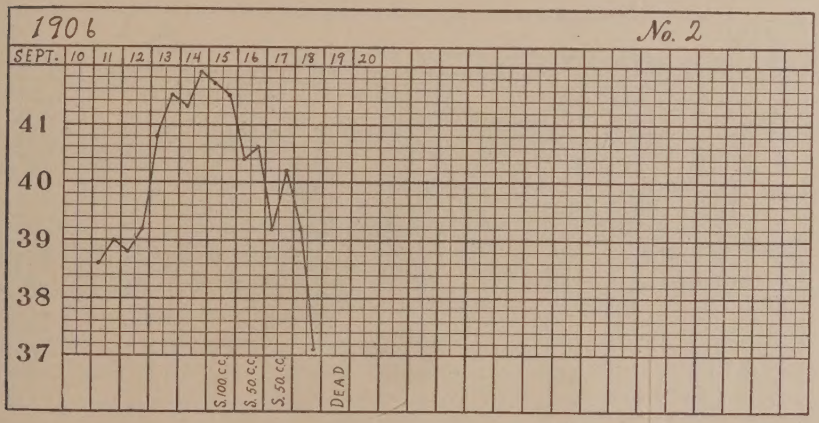
The methods of immunizing cattle, bleeding them and bottling the serum have already been discussed. One other matter of no small importance is the isolation and care of the non-immune cattle which are to be used for virulent blood. One who is familiar with cattle plague understands readily the ease and rapidity with which this disease spreads. The non-immune animals must be quartered some distance from the infected herd, preferably in a stable screened to keep out the birds and flies which might carry the infection. Persons taking care of the animals should not go near those sick nor should they touch the utensils used around them; and the feed and water of the animals must not become soiled with the discharges. There must be no surface drainage from the sick toward the non-immune animals. The stable should be well constructed and kept in a sanitary condition in order to facilitate disinfection after an accidental outbreak of cattle plague.

Besides the apparatus necessary for the preparation of anticattle-plague serum, equipment for microscopic and bacteriologic work is necessary.

ILLUSTRATIONS.

Temperature Charts 1 to 6. 387


1906
No. 1
SEPT. 10 11 12 13 14 15 16 17 18 19 20
41
40
39
38
37
SERUM 100. C.C.
SERUM 50. C.C.
SERUM 50. C.C.
DEAD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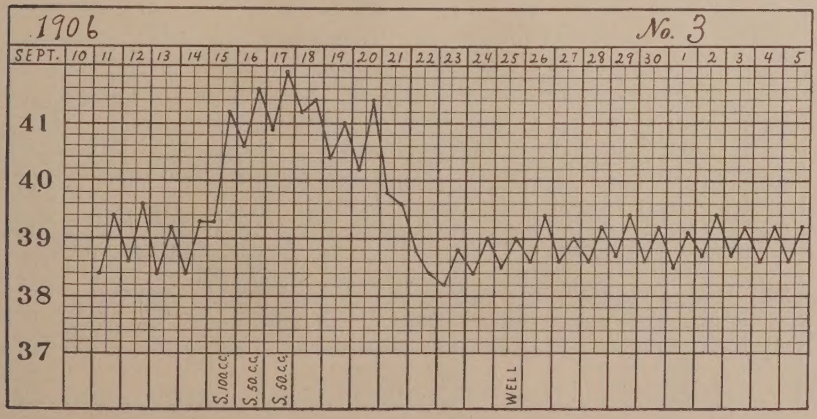
No. 2
SEPT. 10 11 12 13 14 15 16 17 18 19 20
41
40
39
38
37
S. 100 C.C.
S. 50 C.C.
S. 50 C.C.
DEAD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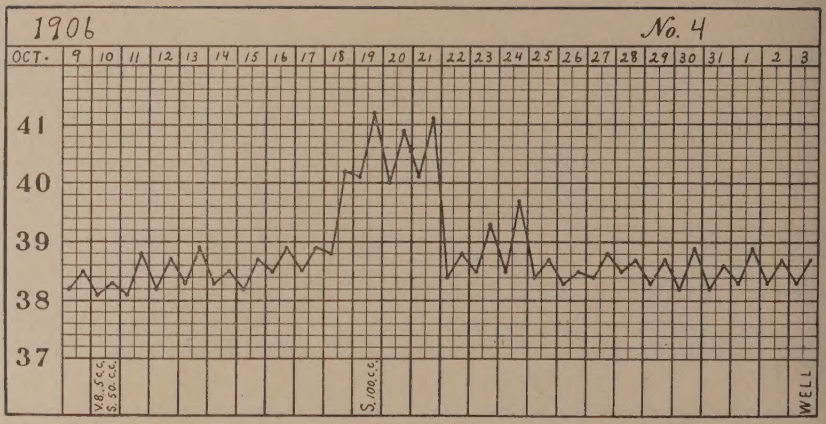
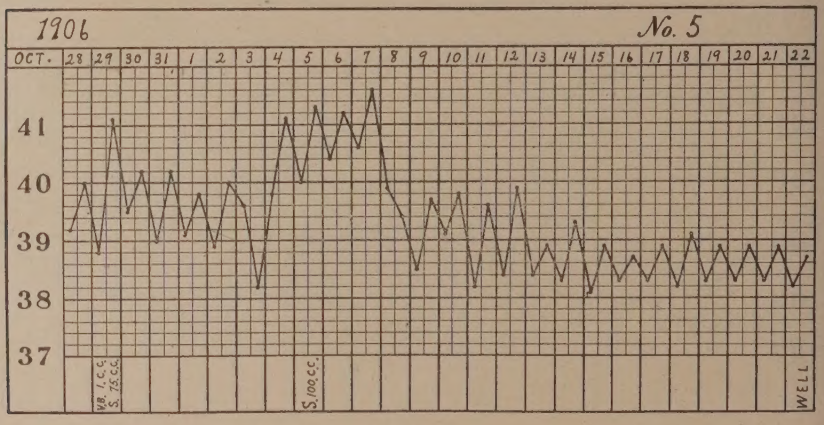
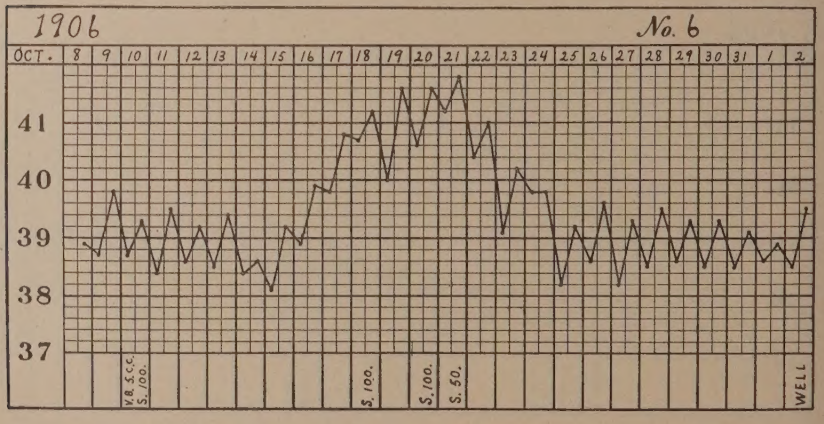
No. 3
SEPT. 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 1 2 3 4 5
41
40
39
38
37
S. 100 C.C.
S. 50 C.C.
S. 50 C.C.
WELL


1906
No. 4
OCT. 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2 3
41
40
39
38
37
V.B. 5 c.c.
S. 50 c.c.
S. 100 c.c.
WELL


1906
No. 5
OCT. 28 29 30 31 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
41
40
39
38
37
V.B. 1 c.c.
S. 75 c.c.
S. 100 c.c.
WELL


1906
No. 6
OCT. 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2
41
40
39
38
37
V.B. 5 c.c.
S. 100.
S. 100.
S. 50.
WELL